State of Art

Health Effects and Sources of Indoor Air Pollution. Part I[1-3]

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Contents

SUMMARY Since the early 1970s, the health effects of indoor air pollution have been investigated with increasing intensity. Consequently, a large body of literature is now available on diverse aspects of indoor air pollution: sources, concentrations, health effects, engineering, and policy. This review begins with a review of the principal pollutants found in indoor environments and their sources. Subsequently, exposure to indoor air pollutants and health effects are considered, with an emphasis on those indoor air quality problems of greatest concern at present: passive exposure to tobacco smoke, nitrogen dioxide from gas-fueled cooking stoves, formaldehyde exposure, radon daughter exposure, and the diverse health problems encountered by workers in newer sealed office buildings. The review concludes by briefly addressing assessment of indoor air quality, control technology, research needs, and clinical implications. AM REV RESPIR DIS 1987; 136:1486-1508

Introduction

During this century, dramatic episodes of excess mortality caused by ambient air pollution convincingly established that atmospheric contamination by human activities can adversely affect health. In many countries, governmental regulations implemented in response to the adverse health effects of air pollution have resulted in strong trends towards improved air quality. As the hazards posed by ambient air pollution from conventional fossil fuels have diminished in some countries, the relevance of indoor air quality for health has become increasingly apparent. Studies of time-activity patterns demonstrate that residents of more developed countries spend on average little time outdoors (table 1) (1, 2). Thus, indoor pollutant concentrations are the predominant determinant of exposure for many pollutants and the only source of exposure for some. However, pollutants in outdoor air do penetrate indoors, and for some pollutants of current importance, such as ozone and acid aerosols, nearly all exposure, whether received indoors or outdoors, results from outdoor sources.

Research directed at indoor air pollution and its adverse health effects began in the late 1960s and early 1970s (3, 4). Investigation in this area was subsequently stimulated by concerns that reduced ventilation of buildings for the purpose of energy conservation would increase pollutant concentrations and lead to adverse effects on health. Consequently, a large body of literature is now available on diverse aspects of indoor air pollution: sources, concentrations, health effects, mitigation, and policy.

While many health effects of indoor air pollution remain controversial, epidemiologic and clinical research has identified some health effects that should be considered by chest physicians and other health care providers. The public has been intensely interested in the new information on indoor air pollution, particularly as it relates to such ubiquitous exposures as formaldehyde, environmental tobacco smoke, radon and radon daughters, nitrogen dioxide (NO_2) from gas-fueled cooking stoves, and smoke from woodburning fireplaces and stoves. Patients may turn to their health care

This is Part I of two parts; the second will appear in the next issue of the Review.

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TABLE 1

AVERAGE HOURS SPENT PER DAY IN VARIOUS LOCATIONS BY ADULTS IN 44 U.S. CITIES*

Location	Employed Men	Employed Women	Housewives
At home	13.4 (55.8)†	15.4 (64.2)	20.5 (85.4)
At work	6.7 (27.9)	5.2 (21.7)	— (0)
In transit	1.6 (6.7)	1.3 (5 4)	1.0 (4.2)
Outside	0.7 (2.9)	0.3 (1.3)	0.4 (1.7)
Inside other structures	1.6 (6.7)	1.8 (7.5)	2.1 (8.8)

* Based on data in tables 7-1.1 and 7-1.3, page 795 in reference 1. Time calculated for "outside" includes the categories "just outside one's home" and "in all other locations." Time calculated for "inside other structures" consists of the categories "in other people's homes," "in places of business," and "in restaurants and bars." The original data did not separate work into indoor and outdoor categories.
† Percentage of 24 h.

providers because of concerns about potential health effects of these and other indoor air pollutants.

The findings reported in this new literature also have wide-ranging policy implications (5). Evidence of adverse health effects of indoor air quality may require decisions and actions on consumer products, building materials and design, energy conservation practices, and regulation of smoking in public places. In the United States, the Environmental Protection Agency under the authority of the Clean Air Act regulates to protect and enhance outdoor but not indoor air quality. This agency has constructed a statutory framework for implementing ambient air quality standards and has devised a complex set of regulations for controlling mobile and stationary air pollution sources.

For some criteria pollutants, an encouraging trend of improving outdoor air quality has resulted. The number of locations exceeding the primary National Ambient Air Quality Standards for total suspended particles (TSP), sulfur dioxide (SO_2), carbon monoxide (CO), and lead (Pb) has decreased over the past decade. Even peak ozone (O_3) concentrations have declined in many locations. Of the 6 criteria pollutants, only NO_2 pollution has worsened (6). However, improvements in ambient air quality do not necessarily imply that human exposures to harmful pollutants have also declined. Indoor air quality is not directly regulated, and use of some sources of indoor air pollution, such as wood stoves and kerosene space heaters, is increasingly widespread. Low air exchange rates in newer homes and office buildings may also increase personal exposures. Thus, air quality policy designed to fully protect public health must address exposures to pollutants indoors as well as outdoors.

This review summarizes information on the health effects of indoor air pollution, with an emphasis on the data that are most relevant for health care providers and those concerned with public health aspects of indoor air quality. We have also focused on the indoor air quality problems of greatest public health concern at present and emphasize those for which new evidence has become available: passive exposure to tobacco smoke, NO_2 exposure from gas-fueled cooking stoves, formaldehyde exposure, radon daughter exposure, and the diverse health problems encountered by workers in newer sealed office buildings. The citations are based primarily on a literature search that extended through June 1986; selected references subsequent to that date have been cited.

Review articles (7–10) and several monographs (11–14) on indoor air pollution have been published, as well as a report by the National Research Council (15). Proceedings of meetings on this topic have also been published (16–24). Numerous sources on the health effects of ambient air pollution are also available, including a statement of the American Thoracic Society (25), reports on individual pollutants by the National Research Council, and the criteria documents prepared periodically by the Environmental Protection Agency.

In this review, we initially consider the sources of indoor air pollution and information on personal exposures to indoor air pollution. Subsequently, for each of the major pollutants, we review the concentrations in indoor environments and the health effects. We conclude by briefly addressing indoor air quality assessment, control technology, research needs, and clinical implications.

Indoor Air Pollution: Sources and Exposure

Introduction

In this section, we highlight information on the sources of those pollutants that have been, or are, potentially associated with disease. We also review studies of personal exposures to pollutants. Concentrations of pollutants in indoor environments are described in subsequent sections on individual pollutants. We do not attempt to cover exhaustively the data on sources and exposures; comprehensive treatments are available in the report of the National Research Council (15) on indoor air pollution, in a review by Yocom (26), and in the proceedings of the Seventh Oak Ridge National Laboratory Life Sciences Symposium (24).

The health risks posed by air pollution are determined by the personal exposure of individuals to contaminants and not simply by pollutant concentrations in indoor and outdoor air. Personal exposures to air pollutants represent the average of the pollutant concentrations encountered in various environments with weighting proportional to the time spent in each location (figure 1). In more developed countries, studies of activity patterns have established the importance of the indoor environment in determining personal exposures (table 1) (1, 2).

The determinants of indoor concentrations vary among the pollutants. Levels may be influenced by outdoor levels, indoor sources, the rate of exchange between indoor and outdoor air, and other characteristics of the structure and its furnishings that influence pollutant dispersion and removal (15). Pollutants from

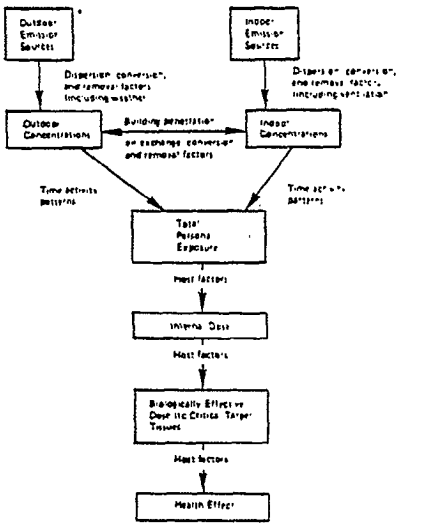

Fig. 1. Framework for considering the relationships among pollutant concentrations, personal exposures doses of pollutants to target tissues, and health effects (Reprinted with permission from reference 27.)

outdoor sources can enter a building through mechanical ventilation systems and through the natural infiltration of air. The indoor concentrations of "outdoor pollutants" depend not only upon the outdoor concentrations but upon the rate of air infiltration, the reactivity of the contaminant, the efficiency of any mechanical filtration systems, and, for solids, upon the particle size and shape. For example, O_3, primarily an ambient pollutant, is a highly reactive molecule; it follows first-order decay kinetics when penetrating indoors and usually reacts quickly with surfaces. Indoor concentrations of O_3 are usually less than 50% of outdoor concentrations (28). Nevertheless, even small amounts of O_3 will be important in some indoor environments, such as art museums and locations with NO_2 sources. The concentrations of pollens, which are large particles from outside sources, decline substantially with increasing distance from doors and windows (29). Outdoor sources may lead to unusually high pollutant levels indoors if fresh air intake vents are improperly located. For example, increased CO levels have been measured in buildings with intake vents fed by air contaminated with vehicle exhaust from adjacent roadways or parking garages.

Increasing concentrations of indoor air pollutants have been of particular concern as ventilation rates have been reduced in newer structures. The 83 million housing units in the United States are diverse in character and some types are more likely to be associated with excessive indoor air pollution than are others. In new "tight" homes, air exchange rates during winter may average less than 0.5 per hour, while most conventional homes have average exchange rates between indoor and outdoor air around 1.0 per hour. Energy efficient "super tight" homes can be built with winter air exchange rates as low as 0.1 to 0.3 per hour. In comparison with conventional homes, mobile homes and prefabricated housing units have lower mean air exchange rates and are of smaller volume. These characteristics make them particularly liable to indoor air pollution problems. In many new office buildings, construction techniques and ventilation practices also lead to low air exchange rates and the potential for air quality problems.

Although most time indoors is spent at home or at work, about 5% of each day is spent in transit (table 1). Transportation environments pose unique problems with regard to air quality. In most, air exchange rates are high, but the ratio of the number of occupants to air volume is much higher than in other environments. For example, commercial jets are designed to have several air exchanges per hour. In an automobile with the windows open or the ventilation fan operating, the number of air exchanges can range from 5 to 50 per hour. The occupant-to-volume ratios are much higher than found in almost every indoor environment used by the general public. Thus, substantial exposure to airborne pollutants may be sustained in transportation environments.

The ventilation systems of commercial aircraft are designed to pressurize the cabin, cool electronic equipment, vent lavatory and galley areas, and provide conditioned air for passenger and crew comfort (30). The air is drawn through compressors, conditioned by mixing with ambient air, and delivered through overhead systems. The air exchange on airplanes is usually quite high, although some aircraft, such as the new Boeing 767, are configured to recirculate 50% of the air. At full passenger load, only 7 cubic feet per minute (cfm) of fresh air per person would be supplied, only slightly greater than the minimum recommended in the current ventilation guidelines of the American Society of Heating, Refrigerating, and Air Conditioning Engineers.

Important and occasionally unique exposures to pollutants can be sustained in special environments, although little time may be spent in these locations on average. For example, sports arenas can be heavily contaminated with tobacco smoke (31), and motorized ice cleaning equipment can increase levels of CO and NO_2 in ice skating rinks (32). Exposure to volatile organic compounds (VOC) can take place in dry cleaning establishments and fabric stores (33). Camping lanterns and cooking stoves are potent sources of NO_2 and CO (34). In fact, fatalities have occurred to campers and explorers from CO poisoning (35, 36).

TABLE 2

TYPICAL SOURCES OF INDOOR AIR POLLUTION IN THE HOME, OFFICE, AND TRANSPORTATION ENVIRONMENT

Environment	Source and Pollutants
Home	Tobacco smoking: respirable particles, CO, VOC*
	Gas stoves: NO_2, CO
	Woodstoves and fireplaces; respirable particles, CO, PAH†
	Building materials: formaldehyde, radon
	Earth underlying the home: radon
	Furnishings and household products: VOC, formaldehyde
	Gas-fueled space heaters: NO_2, CO
	Kerosene-fueled space heaters: NO_2, CO, SO_2
	Insulation: asbestos
	Moist materials and surfaces: biological agents
Office	Tobacco smoking: respirable particles, CO, VOC
	Building materials: VOC, formaldehyde
	Furnishings: VOC, formaldehyde
	Copying machines: VOC
	Air conditioning systems: biological agents, vehicle exhaust with combustion emissions containing particles, CO, and NO_2
Transportation	Tobacco smoking: respirable particles, CO, VOC
	Ambient air: ozone in jet aircraft, CO and lead in automobiles
	Auto air conditioners: biological agents

* Volatile organic compounds
† Polycyclic aromatic hydrocarbons

Sources of Indoor Air Pollution

Numerous sources of airborne contaminants have been identified in indoor environments (tables 2 and 3). The pollutant sources found in home, office, and transportation environments are listed in table 2. In table 3, we describe the sources of the principal pollutants and typical concentrations. Unvented combustion, evaporation of solvents, grinding, and abrasion can produce gaseous and particulate pollution indoors. Radon and its decay products accumulate indoors from soil, water, and building materials. Biological sources include growth of molds, fungi, and bacteria, and insects and pets.

In the home, the principal combustion sources are tobacco smoking, gas cooking stoves, and unvented kerosene heaters. Wood burning in stoves and fireplaces may also affect indoor air quality. Formaldehyde may be released from urea formaldehyde foam insulation (UFFI),

TABLE 3

THE PRINCIPAL INDOOR POLLUTANTS, THEIR SOURCES AND TYPICAL CONCENTRATIONS

Pollutant	Typical Sources	Pollutant Concentrations	Relevant Standards	Comments
Respirable particles	Tobacco smoke, unvented kerosene heaters, wood and coal stoves, fireplaces, outside air, attached facilities, occupant activities	> 500 µg/m³ bars, meetings, waiting rooms with smoking 100 to 500 µg/m³ typical for smoking sections of planes 10 to 100 µg/m³ typical of homes 1,000 µg/m³ with burning food or fireplaces	265 µg/m³ EPA 24-h standard ambient air 75 µg/m³ EPA annual standard ambient air 150 µg/m³ Japanese indoor standard	Current EPA standards are for total, and not only respirable suspended particles
NO, NO_2	Gas ranges and pilot lights, unvented kerosene and gas space heaters, gasoline engines, some gas floor furnaces, outside air	25 to 75 ppb typical range for homes with gas stoves 100 to 500 ppb peak values kitchens with gas stoves or kerosene gas heaters.	160 ppb 1-h maximum, WHO guideline 50 ppb annual average EPA ambient standard	No current EPA short-term standard
CO	Gas ranges and pilot lights, unvented kerosene and gas space heaters, tobacco smoke, back drafting of water heater or furnace or woodstove, gasoline engines, camping lanterns and stoves Attached garages, street level intake vents, hockey rinks	> 50 ppm when oven used for heating > 50 ppm attached garages, air intakes, arenas 2 to 15 ppm cooking with gas stove 2 to 10 ppm heavy smoking in homes, bars, and other locations	35 ppm EPA 1-h standard 9 ppm EPA 8-h standard	
CO_2	People, unvented kerosene and gas space heaters, tobacco smoke, outside air	320 to 400 ppm outdoor air 2,000 to 5,000 ppm crowded indoor environment, inadequate ventilation	1,000 ppm Japanese indoor air standard	CO_2 concentrations below 1,000 ppm usually indicate adequate fresh air supply for buildings.
Infectious, allergenic, irritating biological materials	Dust mites and cockroaches, animal dander, bacteria, fungi, viruses, pollens	Few systematic measurements of spores, bacteria, and viruses indoors Homes with mold problem, offices with water damage* > 1,000 cfu/m³* Homes and offices without obvious problem: 500 ± 200 cfu/m³	None	Interpretations of a level depend on the specific agent; cfu/m is only an indicator
Formaldehyde	Urea formaldehyde foam insulation (UFFI), glues, fiberboard, pressed board, plywood, particle board, carpet backing and fabrics	0.1 to 0.8 ppm homes with UFFI 0.5 ppm average in mobile homes > 1 ppm in a few homes and mobile homes	0.2 to 0.5 ppm adopted by several states 0.1 ppm Sweden, new homes 0.7 ppm Sweden, maximum in old buildings 3 ppm U.S. OSHA 8-h time-weighted average	Formaldehyde concentrations in homes with UFFI decline by 50% every 2 to 3 yr.
Radon and radon daughters	Ground beneath a home, domestic water, and some utility natural gas	1.5 pCi/l estimated average in U.S. homes > 8 pCi/l in 3% to 5% homes	8 pCi/l NCRP action level 4 pCi/l EPA limit for uranium processing site homes 2 pCi/l ASHRAE guidelines 5 pCi/l Sweden, maximum, existing buildings 3 pCi/l Sweden, maximum, new buildings	Radon or radon daughters can be measured. Standards are for radon. Lung cancer risk results from radon daughters.
Volatile organic compounds: benzene, styrene, tetrachloroethylene; dichlorobenzene; methylene chloride; chloroform	Outgassing from water, plasticizers, solvents, paints, cleaning compounds, mothballs, resins, glues, gasoline, oils, combustion, art materials, photocopiers, personal care products	Typical indoor concentrations of selected compounds: benzene—15 µg/m³; 1,1,1 trichloroethane—20 µg/m³; chloroform—2 µg/m³; tetrachloroethylene—5 µg/m³; styrene—2 µg/m³; m,p-dichlorobenzene—4 µg/m³; m,p-xylene—15 µg/m³	No indoor standards for nonoccupational settings	EPA Carcinogenic Assessment Group potency factors available for many of the volatile organics.
Semivolatile organics: Chlorinated hydrocarbons, DDT, heptachlor, chlordane	Pesticides, transformer fluids, termicides, combustion of wood, tobacco, kerosene, and charcoal; wood preservatives, fungicides	Only limited data available	No indoor standards	
Semivolatile organics: polycyclic compounds, benzo(a)pyrene, polychlorinated biphenols	Herbicides, insecticides			
Asbestos	Insulation on building structural components, asbestos plaster around pipes and furnaces, tiles	No systematic measurements to determine typical fiber concentrations. > 1,000 ng/m³ when friable asbestos	2 fibers/cc OSHA 8-h time-weighted average	EPA and state attention has been on schools and office buildings. Domestic problems not evaluated

* cfu/m³ = colony-forming units/m³

from furnishings, and from household products. Volatile organic compounds have numerous sources within the home including tobacco smoking and household products. Radon, emitted by the earth under a home, can enter through cracks in the foundation, crawl spaces, sump holes, and other portals. Building materials, water, and utility natural gas may also be sources of radon.

In offices, tobacco smoking is an important source of respirable particulates. Formaldehyde and other VOC may be given off by building materials, furnishings, paints, waxes, supplies, and clean-

ing solvents. Biological agents, which have proliferated on moist surfaces, may be dispersed by the office heating and cooling systems. Many of these same sources of air contamination are present in transportation environments.

Personal Exposure to Air Pollutants

Measurement of personal exposures to pollutants confirms the contributions of these indoor sources to total pollutant exposures (37). Direct personal monitoring has become possible with the development of passive sampling equipment and lightweight portable pump systems (38, 39). By combining personal sampling or fixed-location sampling with time-activity information, the relative contributions of various locations and sources to personal exposures can be estimated (37). Studies using these techniques have established the importance of indoor sources for exposure to respirable particulates, CO and NO_2.

For example, Spengler and associates (40) evaluated sources of variation in personal exposures to respirable particles among residents of 2 semirural communities in Tennessee. The ambient concentrations and personal exposures were uncorrelated, but the concentration of respirable particulates in the homes explained more than 60% of the variation in personal exposures. Reported tobacco smoke exposure alone accounted for less than 15% of the variability.

Quackenboss and colleagues (41) reported similar results from a study of personal NO_2 exposures of 35 adults and children living in the vicinity of an agricultural community in central Wisconsin. In this population more than 80% of the variance in week-long personal exposure to NO_2 was accounted for by variation in bedroom concentrations. In contrast, the studies of personal exposure have indicated the predominance of outdoor sources for some pollutants, e.g., O_3 (37).

Health Effects of Indoor Air Pollution

Introduction

We have described the sources of indoor air pollution and the principal pollutants that may be found in specific indoor environments. In this section, we address the health effects associated with these pollutants as well as information on the concentrations of the pollutants in indoor air. In discussing their health effects, we have broadly grouped the pollutants by their sources: combustion sources—tobacco smoke, NO_2, CO, and wood smoke; biological sources—infectious agents and allergens; and miscellaneous sources—radon and radon daughters, volatile organic compounds, and formaldehyde. The problem of building-related illnesses or "tight building syndrome," which cannot be linked to specific agents, is described separately. We do not review the hazards, primarily nonrespiratory, of exposure to pesticides. The National Research Council (42) has recently addressed the nonoccupational health risks of asbestiform fibers, and we do not cover this exposure. Finally, we do not consider the effects of pollutants generated by outdoor sources that penetrate indoors nor exposures in the work environment that are associated with well-recognized forms of occupational lung disease.

Tobacco Smoke

Introduction. Extensive toxicologic, experimental, and epidemiologic data, largely collected since the 1950s, have established that active cigarette smoking is a major preventable cause of morbidity and mortality (43). Involuntary exposure to tobacco smoke has only recently been investigated as a risk factor for disease in nonsmokers. Consequently, the evidence on involuntary smoking is more limited in scope than for active smoking, and controversy remains concerning certain associations of involuntary smoking with disease.

Nonsmokers inhale environmental tobacco smoke, the combination of the sidestream smoke that is released from the cigarette's burning end and the mainstream smoke exhaled by the active smoker (44). Comprehensive discussions of the chemistry of sidestream and of mainstream smoke are included in the 1979, 1984, and 1986 reports of the Surgeon General (43, 45, 46), in the 1981 report of the National Research Council on indoor air pollution (15), and in the 1986 report of the National Research Council on environmental tobacco smoke (47).

The exposures of involuntary and active smoking differ quantitatively and, to some extent, qualitatively (15, 45–48). Because of the lower temperature in the burning cone of the smoldering cigarette, most partial pyrolysis products are enriched in sidestream as compared to mainstream smoke. Consequently, sidestream smoke has higher concentrations of some toxic and carcinogenic substances than mainstream smoke; however, dilution by room air markedly reduces the concentrations inhaled by the involuntary smoker in comparison to those inhaled by the active smoker. Nevertheless, involuntary smoking is accompanied by exposure to many of the toxic agents generated by tobacco combustion (15, 45–48). The intake of tobacco smoke components by nonsmokers has been confirmed by studies using biological markers such as nicotine and its metabolite, cotinine. Thus, it is biologically plausible to hypothesize that exposure to environmental tobacco smoke is a risk factor for disease in nonsmokers. Active smokers must necessarily have greater exposure to environmental tobacco smoke than nonsmokers, but the consequences of smokers' active and passive exposures cannot be separately evaluated.

To date, research on passive smoking has focused on respiratory effects, although recent investigations have examined associations with diverse health effects including nonrespiratory cancers, ischemic heart disease, age at menopause (49), sudden infant death syndrome (50), and birth weight (51, 52). This review will emphasize the respiratory effects of involuntary smoking. Because the literature on passive smoking has been reviewed in this journal (53), in the 1984 and the 1986 reports of the Surgeon General (45, 46), and by the National Research Council (47), we will focus on the newer studies and the converging evidence for some effects of involuntary smoking. Symposia (18, 54, 55) and a monograph by Shephard (56) have also addressed the adverse health effects of involuntary smoking. Other reviews on selected aspects of the health effects of involuntary smoking have also been published (57–61).

Exposure to Environmental Tobacco Smoke. Tobacco smoke is a complex mixture of gases and particles that contains myriad chemical species (43, 45). Not surprisingly, tobacco smoking in indoor environments increases levels of respirable particulates, nicotine, polycyclic aromatic hydrocarbons, CO, acrolein, NO_2, and many other substances. The extent of the increase varies with the number of smokers, the intensity of their smoking, the ventilation rate of the indoor space, and the use of air cleaning devices. Several cigarette smoke components have been measured in indoor environments as markers of the contribution of tobacco combustion to indoor air pollution. Particulates have been measured most often; sidestream and mainstream smoke both

contain high concentrations of particles in the respirable size range (46, 47). However, surveys of indoor air quality based on measurement of total suspended particulate concentrations will not readily identify the excess mass indoors from environmental tobacco smoke. Studies of levels of environmental tobacco smoke components have been conducted largely in various public buildings; fewer studies have been conducted in the home and office environments (46, 47).

The contribution of smoking in the home to indoor air pollution has been demonstrated by studies involving personal monitoring and monitoring of homes for respirable particulates. Spengler and associates (62) monitored 80 homes for respirable particulate concentrations over several years and found that a smoker of 1 pack of cigarettes daily contributed about 20 μg/m³ to 24-h indoor particle concentrations. In homes with 2 or more heavy smokers, this study showed that the 24-h National Ambient Air Quality Standard of 260 μg/m³ for total suspended particulates could be exceeded. Because cigarettes are not smoked uniformly over the day, higher peak concentrations must occur when cigarettes are actually smoked. Therefore, short-term total suspended particulate concentrations of 500 to 1,000 μg/m³ are likely at the time when cigarettes are actually smoked. The dramatic effect of smoking in the home is shown in figure 2, which summarizes 24-h samples of respirable suspended particulates in residences (63). The variation in the excess indoor concentrations among residences was related to the number of smokers and the air exchange rates. Home 13 had an average air exchange rate of only 0.44 per hour.

Spengler and associates (40) measured the personal exposures to respirable particulates sustained by nonsmoking adults in 2 rural Tennessee communities. The mean 24-h exposures were substantially higher for those exposed to smoke at home.

Levels of other constituents of tobacco smoke have not been well characterized in homes. In the studies of Moschandreas and associates (63), only homes with smokers had iron, arsenic, and cadmium levels indoors that exceeded outdoor concentrations. Ambient cadmium ranged between 1 and 2.5 ng/m³ while the indoor home average concentrations ranged between 2 and 5 ng/m³ in the homes with heavy smoking. Under usual circumstances of smoking, the average emission rate of CO, 50 mg per cigarette, will not increase concentrations in a residence to the standards set for outdoor air (64).

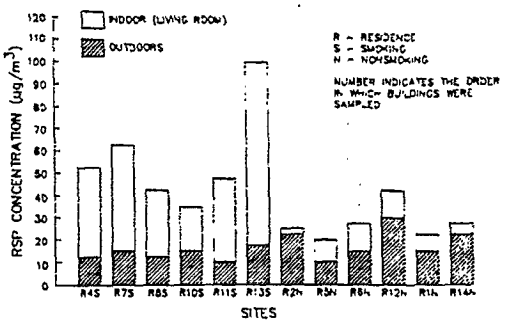

Fig. 2. Average 24-h respirable suspended particulate (RSP) concentrations (μg/m³) outdoors and indoors in homes with and without smokers. (Redrawn with permission from reference 63.)

More extensive information is available on levels of environmental tobacco smoke in various public buildings. Monitoring in locations where smoking may be intense, such as bars and restaurants, has generally shown elevations of particulates and other markers of smoke pollution where smoking is taking place (46, 47). For example, Repace and Lowrey (65) used a piezobalance to sample aerosols in restaurants, bars, and other locations. They found that respirable particulate levels ranged up to 700 μg/m³ and varied with the intensity of smoking. Similar data have been reported for the office environment, though the information is more limited (46, 47).

Transportation environments may also be affected by cigarette smoking. Contamination of air in trains, buses, automobiles, airplanes, and submarines has been documented (46, 47). For example, a recent National Research Council Report (30) on air quality in airliners summarized studies of tobacco smoke pollutants in commercial aircraft. During a single flight, the NO_2 concentration varied with the number of passengers with a lighted cigarette. In another study, respirable particulates in the smoking section were measured at concentrations 5-fold or greater than in the nonsmoking section. Peaks as high as 1,000 μg/m³ were measured in the smoking section.

Markers of Exposure. Biological markers of tobacco smoke exposure have been used to describe the prevalence and the dosimetry of involuntary smoking. In both active and involuntary smokers, the detection of various smoke components or their metabolites in body fluids or alveolar air provides evidence of exposure, and levels of these markers can be used to gauge the intensity of exposure to tobacco smoke. The risks of involuntary smoking have also been estimated by comparing levels of biological markers in active and involuntary smokers.

At present, the most sensitive and specific markers for tobacco smoke exposure are nicotine and its metabolite, cotinine (47, 66). Neither nicotine or cotinine are present in body fluids without exposure to tobacco smoke. Because the circulating half-life of nicotine is generally less than 2 h (67), nicotine concentrations in body fluids reflect recent exposures. In contrast, cotinine has a half-life in the blood or plasma of active smokers that ranges from less than 10 h to about 40 h (68, 69). The half-life of cotinine tends to be longer in nonsmokers than in smokers (68). Hence, cotinine levels provide information about more chronic exposure to tobacco smoke in both active and involuntary smokers. Thiocyanate concentration in body fluids, concentration of CO in expired air, and carboxyhemoglobin level distinguish active smokers from nonsmokers, but these measures are not as accurate as cotinine for assessing involuntary exposure to tobacco smoke (66, 70, 71).

Recent reports described cotinine levels and their relationship to exposure in adult nonsmokers and in children (table 4). In adult nonsmokers, exposures at home, in the workplace, and in other settings determined cotinine concentrations in urine and saliva. The cotinine levels associated with involuntary smoking ranged from less than 1% to about 8% of cotinine levels measured in active smokers. As would be anticipated, smoking by parents was the predominant determinant of the cotinine levels in children. Greenberg and colleagues (75) found significantly higher concentrations of cotinine in the urine and saliva of infants exposed to cigarette smoke in their homes in comparison with unexposed controls. Urinary cotinine levels in the infants increased with the number of cig-

TABLE 4

SELECTED STUDIES OF COTININE LEVELS IN NONSMOKERS

Population	Findings
100 adult patients attending clinics in London (72)	Cotinine levels parallel self-reported exposure. In nonsmoking, mean = 1.5 ng/ml in saliva; in active smokers, mean = 309.9 ng/ml.
151 adult males attending a clinic in London and 70 subjects from Oxford (73, 74)	Urinary cotinine level increased with reported duration of smoke exposure. In nonexposed nonsmokers, median level = 2.0 ng/ml; exposed nonsmokers, median = 6.0 ng/ml; active cigarette smokers, median = 1,645 ng/ml. Smoking by wife increased cotinine concentrations 3-fold in nonsmoking men.
51 infants attending clinics in North Carolina (76).	In nonexposed, median urinary level = 4 ng/mg creatinine; exposed, median = 351 ng/mg creatinine. Salivary creatinine levels higher in exposed.
472 nonsmoking adults in Japan (76).	Exposure at home and at work independently increased urinary cotinine level. In nonsmokers, median = 680 ng/mg creatinine; active smokers, median = 8,570 ng/mg creatinine.
569 schoolchildren, 11 to 16 yr of age, in Bristol, England (77).	Salivary cotinine level increased with the number of smoking parents. If neither parent smoked, median = 0.20 ng/ml; if both smoked, median = 2.70 ng/ml.
38 children, 3 to 15 months of age, attending a child center in North Carolina (78).	Serum cotinine level increased with the number of smokers in the home. In children without household exposure, mean = 1.0 ng/ml, exposed, mean = 4.1 ng/ml.
839 children and adults in a population sample in New Mexico (79)	Salivary cotinine level increased with the number of smokers in the home. If no smokers in the home, median level was zero. If 1 or more smokers, median was greater than zero and increased with the number of smokers.

arettes smoked during the previous 24 h by the mother. The findings were similar in another study of infants that was based on serum cotinine levels (78). Luck and Nau (80) have shown that cotinine and nicotine levels measured in infants breastfed by smoking mothers reflect both the doses received from the breast milk and from involuntary smoking. In a study of schoolchildren in England, salivary cotinine levels rose with the number of smoking parents in the home (77). Similar data were recently reported from a large population-based sample in New Mexico (79).

The results of some investigations based on other markers of exposure have been similar. For example, Poulton and associates (81) reported that serum thiocyanate levels were significantly higher in children living with smokers. In fact, levels of thiocyanate are increased in umbilical cord blood if the mother lives with smokers (82). Nicotine levels in adults vary with report of recent exposure, and in several English studies all nonsmokers had measurable concentrations of nicotine in body fluids (66, 83, 84).

The results of these studies using biological markers have important implications for research on involuntary smoking. The studies provide ample evidence that involuntary exposure leads to absorption, circulation, and excretion of tobacco smoke components, and the studies confirm the high prevalence of involuntary smoking, as ascertained by questionnaire (85). The results further suggest that questionnaire methods for assessing recent exposure have some validity. These studies also demonstrate that saliva and urine samples can be readily obtained from large populations; thus, cotinine levels in body fluids could be used as a marker of exposure in large-scale epidemiologic research on involuntary smoking. However, further investigation is needed to define the relationship between inhaled nicotine and cotinine levels in body fluids, the extent to which cotinine levels index doses of other tobacco smoke components, and the range and determinants of cotinine half-life in nonsmokers. Further, a biological marker for cumulative exposure, which would facilitate investigation of chronic diseases, has not been identified.

Comparisons of levels of biological markers in smokers and nonsmokers have been made in order to estimate the relative intensities of active and involuntary smoking. However, a simple proportionality cannot be assumed between the ratio of the levels of markers in passive and active smokers and the relative doses of all tobacco smoke components. Nonetheless, several investigators have attempted to characterize involuntary smoking in terms of active smoking. For example, Foliart and coworkers (86) measured urinary excretion of nicotine in flight attendants during an 8-h flight and estimated that the average exposure was 0.12 to 0.25 mg of nicotine. Russell and colleagues (87) compared nicotine levels in nonsmokers exposed to tobacco smoke with levels achieved after infusion of known doses of nicotine. On the basis of this comparison, the investigators estimated that the average rate of nicotine absorption was 0.23 mg per hour in a smoky tavern, 0.36 mg per hour in an unventilated smoke-filled room, and 0.014 mg per hour from average daily exposure. In active smokers, the first cigarette of the day resulted in absorption of 1.4 mg of nicotine.

Nonmalignant Respiratory Effects. The 1983 "State of the Art" review on involuntary smoking (53) and the 1984 and the 1986 reports of the Surgeon General (45, 46) provide comprehensive summaries of the literature on respiratory effects of involuntary smoking other than lung cancer. These publications have concurred in concluding that for children passive smoking increases the occurrence of lower respiratory illness, particularly early in life, and increases the frequency of chronic respiratory symptoms. On the basis of primarily cross-sectional data, the 1984 report of the Surgeon General (45) also concluded that the children of smoking parents in comparison with those of nonsmokers had small reductions of lung function, but the long-term consequences of these changes were regarded as unknown. In the 2 yr between the 1984 and the 1986 reports, sufficient longitudinal evidence accumulated to support the conclusion in the 1986 report (46) that involuntary smoking reduces the rate of lung function growth during childhood. Only limited data pertaining to adults have been available, and definitive conclusions have not been made for adult populations.

The more recent data on children have generally supported the conclusions of the earlier review in this journal (53) and of the Surgeon General's reports. With regard to respiratory illness in infants, Pedreira and colleagues (88) prospectively monitored the incidence of lower respiratory illness in 1,144 infants followed in a pediatric practice. Office visits

for tracheitis and bronchitis were significantly more common for infants exposed to tobacco smoke at home. The effects of prenatal smoke exposure could not be separated from those of postnatal exposure in previous studies of lower respiratory illness. However, relevant data have been published from 2 populations. A prospective study in China of 1,058 infants of nonsmoking mothers demonstrated that paternal smoking increased the rate of hospitalization for respiratory illness during the first 18 months of life (89). A British cohort study suggested independent effects of prenatal and postnatal exposure on lower respiratory illness experience in early life (90).

Data from 2 large cross-sectional investigations demonstrated an association between parental smoking habits and lower respiratory illness before 2 yr of age (91, 92). Ware and associates (92) analyzed questionnaire information from 10,106 children, 6 to 9 yr of age at enrollment, who were participating in the Harvard Air Pollution Health Study in 6 U.S. cities. Smoking by both the mother and the father was associated with a higher frequency of reported physician-diagnosed respiratory illness before 2 yr of age. The relative odds for this illness variable increased progressively with the usual number of cigarettes smoked daily by the mother at the time of interview. In a prevalence survey of 1,355 Iowa children 6 to 12 yr of age, parental smoking significantly increased the risk of hospitalization for a chest illness before 2 yr of age (91). Although recall of past illnesses may be inaccurate (93), bias in reporting that depends upon parental smoking habits is unlikely.

Two recent studies did not show effects of involuntary smoking on respiratory illnesses in children. Gardner and colleagues (94) monitored 131 infants during the first year of life for viral infections by serology, cultures, and clinical examinations. Neither specific infections nor illnesses were associated with parental smoking habits. The study population was small, however, and did not have sufficient statistical power to examine effects in the range of interest. In a study based on data from a health maintenance organization, Vogt (95) found that household smoking characteristics did not influence use of outpatient care services for respiratory illness by children.

New studies have showed that children exposed to cigarette smoke in their homes are also at increased risk for middle ear disease. Both acute otitis media (96) and persistent middle ear effusions (97–99) have been associated with involuntary smoking.

The more recent studies continue to indicate increased respiratory symptoms in the children of smokers. In the Harvard Air Pollution Health Study, smoking by parents increased the frequency of cough and wheeze in their children by up to about 30% (92). Analysis of data from 3,482 nonsmoking children, collected in 1962 to 1965 in Tecumseh, Michigan, also indicated more frequent respiratory symptoms in the children of smokers (100, 101). Charlton (102) conducted a survey on cigarette smoking that included 15,709 English children 8 to 19 yr of age. In the nonsmoking children, the prevalence of frequent cough was significantly higher if either the father or the mother smoked, in comparison with the prevalence when neither parent smoked.

The findings of the newer studies are inconsistent on the relationship between passive smoking and wheezing and asthma. McConnochie and Roghmann (103) assessed predictors of wheeze in a retrospective cohort study of children who had mild bronchiolitis in infancy and of control children without illness. At a mean age of 8.3 yr, current exposure to tobacco smoke at home was a significant predictor of wheeze (odds ratio = 1.9, $p = 0.05$). Further analysis of data from the control children showed that maternal smoking significantly increased the prevalence of wheezing on follow-up in children from families with a history of respiratory allergy (104). In the study of children in Tecumseh, Michigan, parental smoking was associated with a higher prevalence of asthma at the initial examination and with a doubling of the risk for developing asthma during the 15-yr follow-up period (100, 101). Murray and Morrison (105) evaluated 94 asthmatic children 7 to 17 yr of age. Level of lung function, symptom frequency, and responsiveness to inhaled histamine were adversely affected by maternal smoking.

In contrast, Tashkin and associates (106) examined cross-sectional data from children 7 to 17 yr of age in the Los Angeles area and found no association between the smoking characteristics within the households and the prevalence of respiratory symptoms or asthma. In a prospective cohort study in New Zealand, parental smoking habits were not found to affect the incidence of asthma during the first 6 yr of life (107). In 1980, Weiss and associates (108) reported the results of a cross-sectional survey of respiratory symptoms in 650 children in Massachusetts. The prevalence of persistent wheeze, the most common symptom, increased significantly with the number of smoking parents but was unrelated to smoking by the children themselves. These investigators subsequently used cold air challenge to assess airways responsiveness in a sample of these children and found that airways reactivity was not related to maternal smoking history (109).

New studies have further documented the adverse effect of parental smoking on children's lung function, and longitudinal evidence on the consequences of passive smoking during lung growth and development was published. In the study of children in Tecumseh, Michigan, parental smoking was associated with reduced lung function, as assessed by spirometry (100, 101). The magnitude of effect varied with age, sex, and the index of exposure to parental smoking. In the survey in Los Angeles, maternal smoking was associated with average reductions of 3 to 8% for spirometric parameters in male subjects (106). The effects of paternal smoking were largest in boys less than 12 yr of age and were variable in girls. Ekwo and coworkers (91) found significantly greater response to inhaled bronchodilator in the children of cigarette smokers. In the Harvard Air Pollution Health Study, the FEV_1 of children whose mothers smoked at the time of spirometry was reduced by slightly less than 1% of predicted FEV_1 reduction (92). In contrast, Hosein and Corey (110) studied 1,357 children and did not find an effect of home exposure to tobacco smoke on FEV_1 level. Lebowitz and colleagues (111) also did not find effects of parental smoking, but only 271 children were included in the study population.

Based on cross-sectional data from children in East Boston, Massachusetts, Tager and associates (112) reported in 1979 that the level of FEF_{25-75} declined with the number of smoking parents in the household. In 1983, these investigators provided the results obtained with follow-up of these children over a 7-year period (113). Using a multivariate technique, Tager and associates showed that both maternal smoking and active smoking by the child reduced the growth rate of the FEV_1. The statistical model predicted effects of maternal smoking that are of a physiologically important magnitude. Lifelong exposure of a child to a smoking mother was estimated to reduce growth of the FEV_1 by 10.7, 9.5,

and 7.0% after 1, 2, and 5 yr of follow-up, respectively.

Recent longitudinal data from the Harvard Air Pollution Health Study also showed reduced growth of the FEV_1 in children whose mothers smoked cigarettes (114). The growth rate of the FEV_1 from ages 6 through 10 yr was calculated for 7,834 white children. Although all representations of exposure to parental smoking were associated with reduced growth rate of the FEV_1, only the level of maternal smoking in packs per day attained statistical significance at $p < 0.05$. From ages 6 through 10 yr, the statistical model estimated that FEV_1 growth rate is reduced by 0.17% per pack of cigarettes smoked daily by the mother. This effect was somewhat smaller than that reported earlier by Tager and associates (113), although if extrapolated to age 20 yr, a cumulative effect of 2.8% is predicted. The 2 sets of data were also analyzed with noncomparable techniques, and the study populations may have differing levels of exposure to passive smoking.

Burchfiel (100, 101) examined the effects of parental smoking on 15-yr lung function change of subjects in the Tecumseh study, first examined at ages 10 through 19 yr. In the female subjects who remained nonsmokers across the follow-up period, parental smoking was not associated with lung function change. In nonsmoking males, parental smoking reduced the growth of the FEV_1, FVC, and $\dot{V}max_{50}$, although the sample size was limited and the effects were not statistically significant. For the FEV_1 in males, the analysis estimated 7.4% and 9.4% reductions in 15-yr growth associated with 1 or 2 smoking parents, respectively.

Some new information has become available for adults since the previous reviews, which cited data from only 4 epidemiologic studies. The ratio of hydroxyproline to creatinine in urine was used by Japanese investigators as a marker of lung injury (115). In women passively exposed to cigarette smoke, this ratio increased with the extent of daily exposure. However, in a study in Germany, the hydroxyproline to creatinine ratio in nonsmokers did not vary with passive smoke exposure (116). Moreover, Read and Thornton (117) reported that in experimental studies with rats, the hydroxyproline to creatinine ratio actually decreased with increasing exposure to smoke. They also reported that in humans both hydroxyproline and creatinine individually increased with increased nicotine absorption from active smoking in males but not in females (117). The ratio of the two, however, was not associated with increased nicotine excretion in either sex.

The results of several of the more recent epidemiologic studies indicate possible chronic effects of passive smoking on lung function in adults. The results of an investigation of 163 nonsmoking women in the Netherlands suggested adverse effects of tobacco smoke exposure in the home (118, 119). Cross-sectional analysis of spirometric data collected in 1982 showed reductions of most parameters in association with tobacco smoke exposure in the home, although the effect was significant only for flows at higher lung volumes. In a sample of the women, domestic tobacco smoke exposure was not associated with longitudinal decline of lung function during the period 1965 to 1982. In baseline data for a cohort study in Scotland, respiratory symptoms tended to be more prevalent in nonsmokers living with smokers in comparison to nonsmokers living with nonsmokers (120).

Other studies have not indicated chronic effects of passive tobacco smoke exposure on adult nonsmokers. Jones and associates (121) conducted a case-control study of 20- to 39-yr-old nonsmoking women in the Tecumseh Community Health Study cohort. Subjects from the highest and lowest quartiles of the lung function distribution had comparable exposure to smokers in the home. Kentner and colleagues (122) in a study conducted in Germany examined the effects of passive and active smoking in 1,351 white collar workers. Self-reported exposure to environmental tobacco smoke at home and at work was not associated with reduction of lung function, as assessed by spirometry. In a small case-control study, marriage to a smoker was not associated with excess risk for chronic bronchitis (123).

New experimental and epidemiologic studies have not consistently shown acute effects of passive smoking on lung function level in asthmatic and nonasthmatic children and adults. As described above, Murray and Morrison (105) found lower ventilatory function in asthmatic children with smoking mothers. In a population sample in Tucson, Arizona, Lebowitz (124, 125) examined the relationship between passive smoking and daily symptom occurrence and daily level of peak flow. Statistically significant effects of tobacco smoke exposure were not found for either outcome in the 229 children and adults. In an experimental study, 1-h chamber exposure of young asthmatics to cigarette smoke did not reduce expiratory flow rates and was, in fact, followed by a small decrease in nonspecific airways reactivity (126).

The accumulating evidence since previous reviews continues to demonstrate adverse effects of passive smoking on the lungs of children. Data from large populations showed significant effects on lung function level and symptom occurrence (91, 92, 102, 106). Results from follow-up of the East Boston, the Harvard, and the Tecumseh study cohorts (100, 101, 113, 114) suggested that the effects on lung function should not be dismissed as clinically insignificant.

Important research questions pertaining to passive smoking and the child's lung remain unanswered, however (46, 127). The mechanisms of injury have not been established, and the relative importance of exposures *in utero*, during infancy, and later in childhood has not been examined. Nevertheless, the available evidence of adverse effects does provide sufficient rationale for intervention. In contrast to the evidence for children, the data on adults are more variable and do not yet permit conclusive statements concerning passive smoking during adulthood and reductions of lung function and increased respiratory symptom occurrence.

Lung Cancer. In 1981, reports were published from Japan (128) and from Greece (129) that indicated increased lung cancer risk in nonsmoking women married to cigarette smokers. Subsequently, this controversial association has been examined in investigations conducted in the United States, Scotland, Japan, and Hong Kong. The association of involuntary smoking with lung cancer derives biological plausibility from the presence of carcinogens in sidestream smoke and the lack of a documented threshold dose for respiratory carcinogenesis in active smokers (130). Further, mutagenic activity can be found in the urine of nonsmokers after passive exposure to tobacco smoke (131, 132).

Time trends of lung cancer mortality in nonsmokers have been examined with the rationale that temporally increasing exposure to environmental tobacco smoke should be paralleled by increasing mortality rates. Enstrom (133) calculated nationwide lung cancer mortality rates for 1914 to 1968 and concluded that a real increase had occurred among nonsmoking males after 1935. However, occupational and environmental exposures

TABLE 5

COHORT AND CASE-CONTROL STUDIES OF PASSIVE EXPOSURE TO TOBACCO SMOKE AND LUNG CANCER

Study	Findings	Comment
Prospective cohort study in Japan of 91,540 nonsmoking females, 1966–1981 (136).	Age-occupation adjusted SMR,* by husband smoking: Nonsmokers—1.00 Ex-smokers—1.36 < 20/day—1.45 ⩾ 20/day—1.91	Trend statistically significant. All histologies.
Case-control study in Greece of 40 nonsmoking female cases, 149 controls, 1978–1980 (129)	Odds ratios by husband smoking: Nonsmokers—1.0 Ex-smokers—1.8 Current smokers ⩽ 20/day—2.4 > 20/day—3.4	Trend statistically significant. Histologies other than adenocarcinoma and bronchioloalveolar carcinoma.
Prospective cohort study in the U.S. of 176,139 nonsmoking females, 1960–1972 (134).	Age-adjusted SMR, by husband smoking: Nonsmokers—1.00 Current smokers < 20/day—1.27 ⩾ 20/day—1.10	All histologies. Effect of husband smoking not significant
Case-control study in Hong Kong of 84 female cases and 139 controls, 1976–1977 (137, 138).	Crude odds ratio of 0.75 associated with smoking spouse	All histologies. Two reports are inconsistent on the exposure variable.
Case-control study in the U.S with 22 female and 8 male nonsmoking cases. 133 female and 180 male controls (139).	Odds ratios by spouse smoking: Nonsmokers—1.00 < 40 pack years—1.48 ⩾ 41 pack years—3.11	Significant increase for > 41 pack years. Bronchioloalveolar carcinoma excluded.
Case-control study in the USA. 25 male and 53 female nonsmoking cases with matched controls, 1971–1980 (140).	Odds ratio not significantly increased for current exposure at home: Males—1.26 Females—0.92	All histologies Findings negative for spouse smoking variable as well.
Prospective cohort study in Scotland of 8,128 males and females, 1972–1982 (120).	Age-adjusted mortality ratios for domestic exposure: Males—3.25 Females—1.00	Preliminary, small numbers of cases.
Case-control study in Hong Kong with 88 nonsmoking female cases, 1981–1982 (141, 142).	Odds ratio of 1.24 ($p > 0.40$) for combined home and workplace exposure. No association with cumulative hours of exposure.	All histologies
Case-control study in the U.S. with 31 nonsmoking and 189 smoking female cases (143)	No significant effects of exposure from parents, spouse, or workplace in smokers and nonsmokers.	Adenocarcinoma and squamous cell carcinoma only.
Case-control study in the U.S. with 134 nonsmoking female cases (135)	Nonsignificant odds ratio of 1.22 if husband smoked. Significantly increased odds ratio of 2.11 if husband smoked 20 or more cigarettes daily at home. Significant trend with number of cigarettes smoked at home by the husband.	All histologies Careful exclusion of smokers from the case group.
Case-control study in England with 15 male and 32 female nonsmoking cases, and 30 male and 66 female nonsmoking controls (123).	Overall odds ratio for spouse smoking of 1.1.	Hospital-based study.
Case-control study in Japan with 19 male and 94 female nonsmoking cases, and 110 male and 270 female nonsmoking controls (144).	For females, odds ratio of 1.5 if husband smoked, for males, odds ratio of 1.8 if wife smoked.	Clinical or radiologic diagnosis for 43%. All histologies.
Case-control study in Louisiana, Texas, and New Jersey with 99 nonsmoking cases and 736 controls (145).	Adjusted odds ratio for marriage to a smoking spouse was 1.5.	Nearly 100% histologic confirmation All histologies.
Case-control study in New Mexico with 28 nonsmoking cases and 292 nonsmoking controls (146).	Adjusted odds ratio for marriage to a smoking spouse was 3.2. No effect in active smokers.	All histologies other than bronchioloalveolar carcinoma.

* Standardized mortality ratio

other than environmental tobacco smoke could explain the apparent mortality rate increase in males. Garfinkel (134) did not identify similar trends in nonsmokers in the Dorn study of male U.S. veterans, 1954 to 1969, nor in the American Cancer Society's study of males and females, 1960 to 1972.

Epidemiologists have tested the association between lung cancer and involuntary smoking using conventional designs: the case-control and cohort studies. The results of both study designs may be affected by inaccurate assessment of exposure to environmental tobacco smoke, by inadequate information on personal smoking habits that leads to classification of smokers as nonsmokers, and by the misdiagnosis of a cancer at another site as primary cancer of the lung. For example, in the case-control study reported by Garfinkel and colleagues (135), 13% of cases originally diagnosed as lung cancer were reclassified to other sites after histological review and 40% of the cases initially classified as nonsmokers by chart review were found to be smokers on interview. The difficulty of accurately estimating exposures with questionnaires and descriptions of a spouse's smoking may partly explain the variable findings of the published studies. In fact, the validity and reliability of questionnaires on involuntary smoke exposure have yet to be comprehensively evaluated.

The evidence from the case-control and the cohort studies does not uniformly indicate increased lung cancer risk in persons exposed to environmental tobacco smoke, but most of the studies indicate increased risk in nonsmokers married to smokers (table 5). Hirayama

(128) conducted a prospective cohort study of 91,540 nonsmoking women in Japan. Standardized mortality ratios for lung cancer increased significantly with the amount smoked by the husbands. The findings could not be explained by confounding factors and were unchanged when follow-up of the study group was extended (136). After its publication, this article received intensive scrutiny, and correspondence in the *British Medical Journal* raised concerns about statistical methodology, population selection, uncontrolled confounding, and the seemingly high relative risk; in his responses, Hirayama satisfactorily rebuffed most of these criticisms, although he could not eliminate the possibility of unreported smoking by women classified as nonsmokers (147). Based on the same cohort, Hirayama has also reported significantly elevated standardized mortality ratios for lung cancer of 2.1 and 2.3 in nonsmoking men with wives smoking 1 to 19 cigarettes and 20 or more cigarettes daily, respectively (136).

In 1981, Trichopoulos and colleagues (129) also reported increased lung cancer risk in nonsmoking women married to cigarette smokers. These investigators conducted a case-control study in Athens, Greece, that included cases with a diagnosis other than adenocarcinoma or bronchioalveolar carcinoma and controls selected at a hospital for orthopedic disorders. The findings were unchanged with expansion of the study population (148).

The results of other subsequently reported case-control studies have also demonstrated statistically significant associations between involuntary smoking and lung cancer (135, 144–146) (table 5). The findings from the more recent reports greatly strengthen the evidence from the earlier studies. Several of the newer studies included relatively large numbers of nonsmokers (135, 144, 145). Furthermore, in most of these studies, involuntary smoking was assessed in greater detail than in the earlier reports so that exposure-response relationships could be more fully examined.

The results of 2 other investigations have also been interpreted as showing an increased lung cancer risk associated with passive smoking, although both have methodologic limitations. In Germany, Knoth and colleagues (149) described a series of 59 female lung cancer cases of which 39 were in nonsmokers. Based on census data, the report by Knoth and colleagues projected that a much greater than expected proportion of these nonsmokers had lived in households with smokers. This report did not include an appropriate comparison series, however, and the suitability of substituting census data was not addressed by the authors. In another recent report, Gillis and associates (120) described the preliminary results of a cohort study of 16,171 males and females in western Scotland; domestic exposure to tobacco smoke increased the lung cancer risk for nonsmoking men but not for women. The report was based on only 16 cases of lung cancer in nonsmokers, however.

The results of other investigations indicate lesser or no effects of exposure to environmental tobacco smoke (table 5). In these studies, however, confidence limits for the relative risks associated with marriage to a smoker are wide and overlap with the confidence limits in the studies with significant results (47). Two separate case-control studies in Hong Kong, where lung cancer incidence rates in females are particularly high, did not indicate excess risk from passive smoking (137, 138, 141, 142). In the more recent of the 2 studies, the questionnaire comprehensively assessed cumulative exposure from home and workplace sources (141, 142). Lee and colleagues (123) reported a hospital-based case-control study in England. Although the investigators considered that their findings indicated little or no effect of involuntary smoking, the case series was small.

The results of the American Cancer Society's prospective cohort study of mortality in 176,139 nonsmoking women have also been construed by many as negative (134). However, the standardized mortality ratios for the nonsmoking women with husbands who smoked were greater than unity but not significantly greater. Repace (150) has suggested that the mortality ratios in the American Cancer Society cohort have been reduced by misclassification introduced by workplace exposures, a factor not considered in the original analyses. Recent and preliminary results from a nationwide case-control study also did not demonstrate increased lung cancer risk from domestic exposure to tobacco smoke (140). In another case-control study that was performed in Los Angeles, Wu and colleagues (143) did not find significantly increased risk for adenocarcinoma associated with involuntary smoking in smoking and nonsmoking women. These investigators estimated exposure from parental smoking, spouse smoking, and workplace sources. The relative risk for lung cancer was slightly, but not significantly, increased by exposure from spouse smoking and from smoking by coworkers.

At present, relatively few investigations provide data on the hypothesis that involuntary smoking is a risk factor for lung cancer. The extent of data contrasts with the more extensive literature cited in the 1964 Surgeon General's Report, which characterized active cigarette smoking as a cause of lung cancer (151). The variability of the data on involuntary smoking also contrasts with that on active smoking. However, most of the studies on involuntary smoking and lung cancer have small numbers of cases, and confidence intervals for the effect of involuntary smoking in the various studies would overlap. Variation in the results of the studies may also reflect random and nonrandom errors in the classification of exposure to environmental tobacco smoke. In fact, the problems of dose estimation seem more difficult for lung cancer than for other health effects of involuntary smoking. The relevant exposures may begin at birth and occur under a wide variety of circumstances. Thus, some inconsistency of the studies would be anticipated.

In spite of the variable epidemiologic evidence, environmental tobacco smoke has been recently characterized as a respiratory carcinogen. The International Agency for Research on Cancer of the World Health Organization (152) has concluded that "passive smoking gives rise to some risk of cancer." The agency supported this conclusion in its monograph on tobacco smoking by citing the characteristics of sidestream and mainstream smoke, the absorption of tobacco smoke materials during involuntary smoking, and the nature of dose-response relationships for carcinogenesis. Appropriately, the International Agency for Research on Cancer argued on the basis of biological plausibility rather than on the basis of epidemiologic evidence.

The National Research Council (47) and the U.S. Surgeon General (46) have also concluded that involuntary smoking increases the incidence of lung cancer in nonsmokers. In reaching this conclusion, the National Research Council (47) cited the biological plausibility of an association between environmental tobacco smoke exposure and lung cancer and the supporting epidemiologic evidence. This report carefully considered the sources of bias that may have affected the epidemiologic studies. Based on a

pooled analysis of the epidemiologic data and adjustment for bias, the report's authors concluded that the best estimate for the excess risk of lung cancer in nonsmokers married to smokers was 25%. The 1986 report of the Surgeon General (46) characterized involuntary smoking as a cause of lung cancer in nonsmokers. This conclusion was based on the extensive information already available on the carcinogenicity of active smoking, on the qualitative similarities between environmental tobacco smoke and mainstream smoke, and on the epidemiologic data on involuntary smoking.

The extent of the lung cancer hazard associated with involuntary smoking in the United States remains uncertain, however (46, 153). The epidemiologic studies provide varying and imprecise measures of risk, and dosimetric aspects of involuntary smoking in the respiratory tract are not yet well understood. Risk estimation procedures have been used to describe the lung cancer risk associated with involuntary smoking, but assumptions and simplifications must be made in order to use this method. For example, Repace and Lowrey (154) have recently calculated that approximately 5,000 lung cancer deaths occur annually in U.S. nonsmokers as a result of involuntary smoking. The results of more refined risk estimation models should be forthcoming.

Other Cancers. Recent reports suggest that environmental tobacco smoke exposure may increase risk of cancer at sites other than the lung. One study found that in children, maternal exposure to environmental tobacco smoke during pregnancy was associated with increased risk of brain tumors (155), and in another study paternal but not maternal smoking increased the risk of childhood rhabdomyosarcoma (156). Such effects might arise from smoking-induced changes in germ cells of the parents or through transplacental exposure rather than as a direct effect of smoke inhalation (157, 158).

In adults, involuntary smoking was linked to a generally increased risk of malignancy and to excess risk at specific sites. Miller (159) interviewed surviving relatives of 537 deceased nonsmoking women in western Pennsylvania concerning the smoking habits of their husbands. A significantly increased risk of cancer death (odds ratio = 1.94, $p < 0.05$) was found in women who were married to smokers and were also not employed outside their homes. The large number of potential subjects who were not interviewed and the possibility of information bias detract from this report.

Sandler and colleagues (160–162) conducted a case-control study on the effects of childhood and adulthood exposures to environmental tobacco smoke on the risk of cancer. The 518 cases included all cancers other than basal cell cancer of the skin; the cases and the matched controls were between 15 and 59 yr of age. For all sites combined, significantly increased risk was found for parental smoking (crude odds ratio = 1.6) and for marriage to a smoking spouse (crude odds ratio = 1.5); the effects of these 2 exposures were independent (162). Significant associations were also found for some individual sites: for childhood exposure (161), maternal and paternal smoking increased the risk of hematopoietic malignancy, and for adulthood exposure (160), spouse's smoking increased the risk for cancers of the female breast, female genital system, and the endocrine system. These findings are primarily hypothesis generating and require replication. In a case-control study, such as reported by Sandler and colleagues, biased information on exposure to environmental tobacco smoke is of particular concern. Hirayama (136) has reported significantly increased mortality from nasal sinus cancers and from brain tumors in nonsmoking women married to smokers in the Japanese cohort. In a case-control study of bladder cancer, involuntary smoke exposure at home and at work did not increase risk (163).

These associations of involuntary smoking with cancer at diverse nonrespiratory sites cannot be readily supported with arguments for biological plausibility. Increased risks at some of the sites, e.g, cancer of the nasal sinus and female breast cancer, have not been observed in active smokers (130). In fact, the International Agency for Research on Cancer has concluded that effects would not be produced in passive smokers that would not be produced to a larger extent in active smokers (152).

Cardiovascular Disease. While extensive data establish active cigarette smoking as a causal risk factor for cardiovascular diseases (164), only a few studies have addressed involuntary smoking as a risk factor for these diseases. In the cohort of nonsmoking Japanese women, Hirayama (165) found a small but statistically significant increased risk of death from ischemic heart disease associated with the husband's smoking. Garland and associates (166) prospectively determined mortality from ischemic heart disease in nonsmoking older women residing in southern California. After adjustment for established risk factors, marriage to a smoking spouse was associated with a relative risk of 2.7 ($p < 0.10$). Gillis and colleagues (120) assessed the baseline prevalence of cardiovascular symptoms and major electrocardiographic abnormalities in a population sample residing in Scotland and then determined cause-specific mortality for up to 10 yr of follow-up. In their preliminary report, involuntary smoking was not associated with the prevalence of cardiovascular symptoms at baseline nor with cardiovascular mortality on follow-up. A case-control study in England did not show increased risk for ischemic heart disease or for stroke in nonsmokers married to smokers (123).

Total Mortality. Two cohort studies, the previously mentioned study in Scotland (120) and an investigation of civil servants and their spouses in Amsterdam (167), provided information on involuntary smoking and mortality from all causes. In the Scottish study, total mortality was increased for women living with a smoker but not for men (120). In contrast, mortality was not increased for nonsmoking female subjects in the study in Amsterdam (167). Neither study directly controlled for other factors that influence total mortality.

Summary. The effects of active smoking and the toxicology of cigarette smoke have been comprehensively examined. When considered in the context of that extensive information, the evidence on involuntary smoking supports conclusions concerning certain health effects. In children, involuntary smoking increases the occurrence of lower respiratory illness during infancy, increases the frequency of chronic respiratory symptoms, and reduces the level of lung function. In adults, involuntary smoking is a cause of lung cancer, but associations with other diseases have not been unequivocally established.

Nitrogen Dioxide

Introduction. Nitrogen dioxide causes lung damage at high concentrations (168, 169), but effects at levels currently encountered in outdoor and indoor air have been difficult to characterize. Early studies focused on the health effects of ambient NO_2 (25). However, in the late 1970s, investigators recognized that indoor NO_2 sources were also contributing to personal exposure and that indoor concentrations often exceeded outdoor concentrations in many homes (15). Consequently, more recent studies have em-

TABLE 6

EFFECTS OF GAS COOKING ON RESPIRATORY ILLNESSES AND SYMPTOMS IN CHILDREN

Study Population	Outcome Measure	Results
British Studies:		
5,758 children, 6 to 11 yr of age, England and Scotland (178).	Major respiratory symptoms and diseases individually and as a single composite variable describing the presence of any 1 of 6 symptoms or diseases.	Significant associations with gas cooking of selected symptoms and diseases, and of a composite variable.
2,408 children, 42% of original 5,758 in above study (179).	Single composite variable as described above.	Relative risk for composite variable generally exceeded 1.0; risk varied and decreased with age.
4,827 children, 5 to 11 yr of age, England and Scotland (179).	Single composite variable as described above.	Significant effect of gas stoves on composite variable in urban areas only
808 children, 6 to 7 yr of age, United Kingdom (180).	Single composite variable as described above.	Borderline significant association between composite variable and gas stoves. Increased prevalence as bedroom NO_2 levels increased in a sample with measurements ($n = 80$).
191 children, 5 to 6 yr of age, England (181).	Single composite variable as described above.	No significant association between bedroom NO_2 levels and prevalence of composite variable.
390 infants, 0 to 1 yr of age, England (182).	Respiratory illnesses and symptoms requiring physician visits, assessed prospectively.	No association between gas stove use and respiratory illnesses and symptoms.
1,565 infants, 0 to 1 yr of age, England (183).	Respiratory illnesses and hospitalizations assessed prospectively to 1 yr.	No significant association between illness or hospitalizations and use of gas for cooking
Ohio Studies		
441 upper-middle class families including 898 children less than 16 yr of age (184).	Incidence of acute respiratory illness, determined by bi-weekly telephone calls.	Respiratory illness incidence similar in homes using gas and electric stoves.
120 families from first study, including 176 children less than 12 yr of age (185)	Incidence of acute respiratory illness, determined by bi-weekly telephone calls and validated by home visits.	Respiratory illness incidence similar in homes using gas and electric stoves.
Harvard Air Pollution Health Study		
8,120 children, 6 to 10 yr of age, 6 U.S cities (186, 187).	History of MD diagnosed bronchitis, of serious respiratory illness before age 2, of respiratory illness in last year	Significant association between current use of gas stove and history of respiratory illness before age 2 (odds ratio = 1.23)
10,106 children, 6 to 10 yr of age, 6 U.S cities Expansion of above study (92).	Same as above.	Odds ratio for history of respiratory illness before age 2 decreased to 1.12 ($p = 0.07$).
Other Studies		
676 children, 3rd and 4th grades, Arizona (188).	Prevalence of asthma, wheeze, sputum, cough as determined by parent-completed questionnaire.	Significant association between use of gas stove and prevalence of cough (prevalence rate ratio = 1.97).
4,071 children, 5 to 14 yr of age, Pennsylvania (189).	Major respiratory illnesses and symptoms as determined by parent-completed questionnaire.	No significant association between use of gas stove and any symptom or illness variable
1,138 children, 6 to 12 yr of age, Iowa (91).	Major respiratory symptoms and illnesses as determined by parent-completed questionnaire	Significant association between current gas stove use and hospitalization for respiratory illness before age 2 (odds ratio = 2.4)
121 children, 0 to 13 yr of age, Connecticut (190)	Number of days of illness.	Number of days of illness associated with average hours of heater use
231 children, 6 yr of age, Netherlands (191).	Comparison of NO_2 levels in homes of cases (children with asthma) and controls	NO_2 distributions similar in homes of cases and controls

phasized sources and effects of indoor NO_2 concentrations.

Exposure. Combustion of gas during cooking and the burning of pilot lights releases nitric oxide (NO), NO_2, CO, CO_2, and water. On average, normal use of an unvented gas cooking range adds 25 parts per billion (ppb) of NO_2 to the background concentration in a home (170). The increase is greater during cold weather when the air exchange rate is usually reduced. During cooking with a gas range, peak levels in the kitchen may reach 200 to 400 ppb (10). Therefore, measured personal exposures to NO_2 are higher for persons living in homes with gas stoves than for persons living in homes with electric stoves (26, 41, 170).

Exposure to NO_2 from gas cooking stoves and ovens is widespread. About 50% of homes in the United States have gas cooking appliances; in some urban areas, such as Los Angeles, more than 90% of homes are equipped with gas appliances (171). The potential importance of NO_2 exposure indoors for health is underscored by comparison of the federal standard set for ambient air, 50 ppb annual average, with levels measured in homes with gas cooking appliances. Sexton and associates (172) used data generated by personal, indoor, and outdoor monitoring to develop a computer model for personal and indoor exposure. The model was applied to residents of 6 U.S. cities. Although none of the cities experienced concentrations above the federal standard in outdoor air, the model predicted that more than 25% of the residents of homes with gas ranges would have annual personal exposures over 50 ppb if ambient NO_2 concentrations averaged 30 ppb.

Health Effects. Most studies of the relationship between residential exposure to NO_2 and health have focused on respiratory symptoms and illnesses and on level of pulmonary function. Experimen-

TABLE 7

EFFECTS OF GAS COOKING ON LUNG FUNCTION IN CHILDREN

Study Population	Lung Function Measure	Results
808 children, 6 to 7 yr of age, United Kingdom (180).	PEFR, $FEV_{0.75}$, FEF_{25-75}	No association with NO_2 levels or presence of gas stove.
898 children, 0 to 15 yr of age, from 441 families, Ohio (184).	FVC, $FEV_{0.75}$	Data on children not presented separately. No association with presence of a gas stove.
8,120 children, 6 to 10 yr of age, 6 U.S. cities (186, 187).	FVC, FEV_1	Overall reduction of 16 ml and 18 ml, respectively, for FEV_1 and FVC in children from homes with gas stoves.
16,689 children, 6 to 13 yr of age, 7 areas in U.S. (192).	$FEV_{0.75}$	Significant reduction of 19 ml associated with gas stove use in older girls only.
676 children, 3rd and 4th graders, Arizona (188)	FEV_1	No effect of gas stoves on pulmonary level or rate of growth.
183 children, 6 to 12 yr of age, Iowa (91).	FEV_1, FEF_{75}, FEF_{25-75}	No change after isoproterenol challenge in children from homes with gas stoves.
9,720 children, 6 to 10 yr of age, 6 U.S. cities (92).	FEV_1, FVC	Significant reduction in FEV_1 of 0.6% and FVC of 0.7%. Not significant after adjustment for parental education.
3,175 children, 5 to 14 yr of age, Pennsylvania (193).	FVC, $FEV_{0.75}$, FEF_{25-75}, $Vmax_{75}$, $Vmax_{50}$	No association with use of gas stove

tal investigations support the choice of these outcome measures; NO_2 may damage the lung directly through its oxidant properties or indirectly by increasing susceptibility to respiratory infections (169, 173). In animal models, NO_2 reduces the efficacy of specific lung defense mechanisms, and effects on mucociliary clearance, the alveolar macrophage, and the immune system have been demonstrated (169, 174, 175).

Data on the health effects of NO_2 concentrations likely to be encountered by the general population are derived from experimental and epidemiologic studies. The results of some human exposure studies imply that levels comparable to those measured in homes may increase airways reactivity in some asthmatics, but the results of other studies are inconsistent (175–177). Although experimental studies are useful for describing effects of controlled exposures, they cannot address the issue of chronic effects from chronic lower level exposures. Numerous epidemiologic investigations have now been carried out to assess their relationship.

The majority of these investigations were cross-sectional surveys of schoolchildren (tables 6 and 7). The investigators generally assessed current symptom status and retrospective illness histories, as obtained by parent-completed questionnaire, and pulmonary function. Although NO_2 levels were measured in several of the investigations (180, 181, 194), exposure was most often assessed by simple questions concerning type of fuel used for cooking. Consistent evidence of excess respiratory symptoms and illnesses in children exposed to gas stoves has not been demonstrated (table 6).

Early reports from two cross-sectional surveys of schoolchildren in Great Britain indicated that children from homes with gas stoves had a higher prevalence of respiratory symptoms than children from homes with electric stoves (178, 179). When one of the survey groups was followed longitudinally, however, the relative risks associated with gas stove use became highly variable and tended to decrease as the children grew older (179). These same British investigators surveyed a third group of 808 schoolchildren, and measured NO_2 concentrations in the homes of a small sample ($n = 80$ or 103). The prevalence of respiratory symptoms was higher in children from homes where gas was used for cooking and increased with higher bedroom NO_2 concentrations, although both effects were of borderline statistical significance (180). A similar association between measured NO_2 and respiratory symptoms was not replicated, however, when these same investigators subsequently studied another sample of 183 children (181). Two prospective studies of infants in Great Britain also failed to demonstrate an association between the use of gas for cooking and respiratory illness (182, 183).

Data on children from the United States are similarly inconsistent. Two large cross-sectional studies, one involving the Harvard Air Pollution Health Study (186, 187) and the other involving schoolchildren in Iowa (91), have demonstrated that reports of serious respiratory illness before 2 yr of age (186, 187) and hospitalization for respiratory illness before 2 yr of age (91) were more common among children from homes with gas stoves. When the original cohort in the Harvard Air Pollution Health Study was expanded, however, the odds ratio of 1.23 for serious respiratory illness before 2 yr of age decreased to 1.12 ($p = 0.07$). In the study of Ekwo and associates (91), the effect of exposure to a gas stove varied strongly and inconsistently with parental smoking habits. The effect was absent in homes where 1 parent smoked, largest where both parents smoked, and intermediate where neither smoked. This pattern of interaction cannot be readily interpreted biologically. Schenker and colleagues (189) found no association between type of cooking stove and current respiratory symptoms or previous illness history in a cross-sectional survey of 4,071 schoolchildren in western Pennsylvania.

The relationship between stove type and respiratory illness has also been studied prospectively. Keller and colleagues (184, 185), in a study of 1,952 family members of all ages in Ohio, found that respiratory illness incidence did not vary with stove type. More recently, Berwick and coworkers (190) followed 121 children for 3 months, 59 from homes with kerosene heaters and 62 from homes without such heaters. In a preliminary analysis of their data, they found that hours of heater use, which correlated strongly ($r = 0.70$) with 1-wk integrated NO_2 measurements, was significantly associated with the occurrence of illness lasting for 1 or more days.

The data concerned with lung function level in children are similarly inconclusive (table 7). Of the 4 investigations with large sample sizes (92, 186, 192, 193), 2 have demonstrated small but statistically significant effects of exposure to a gas stove (186, 192). In initial cross-sectional analysis of data from the Harvard Air Pollution Health Study, Speizer

TABLE 8

EFFECTS OF GAS COOKING ON PULMONARY ILLNESS, SYMPTOMS, AND FUNCTION OF ADULTS

Study Population	Outcome Measure	Results
441 upper-middle class families, including 1,054 adults over 15 yr, Ohio (184).	Incidence of acute respiratory illness, determined by biweekly telephone calls.	Respiratory illness incidence similar in homes using gas and electric stoves.
120 families from first study, including 269 adults over 18 yr, Ohio (185).	Incidence of acute respiratory illness, determined by biweekly telephone calls and validated by home visit.	Respiratory illness incidence similar in homes with gas and electric stoves.
1,724 adults, ages ≥ 20 yr, Maryland (195).	Major chronic respiratory symptoms, FEV_1, FVC.	Association between gas stove use and increased prevalence of respiratory symptoms, FEV_1 < 80% predicted, FEV_1/FVC < 70%, found in nonsmoking males only.
708 adults, ages ≥ 20 yr. Nonsmoking sample of above population (196).	Major chronic respiratory symptoms, FEV_1, FVC.	Significant association between gas stove use and increased prevalence of chronic cough and phlegm, low FEV_1/FVC.
102 nonsmoking women in lowest quartile of FEV_1 compared to 103 nonsmoking women in highest quatrile, Michigan (121).	Comparison of proportions of cases and controls currently using gas stoves.	Marginal association between use of gas stove and lower lung function, (odds ratio = 1.8, p = 0.08).
97 nonsmoking adult females, Netherlands (194).	IVC, FEV, FVC, PEF, MEF_{75}, MEF_{25}, MMEF.	Cross-sectional analysis showed an association between current NO_2 exposure and decreases in most pulmonary function measures. No association with longitudinal decline in pulmonary function.

and associates (186) demonstrated average reductions, adjusted for parental smoking and socioeconomic status, of 16 ml and 18 ml in the FEV_1 and the FVC, respectively, in children from homes with gas stoves compared to children from homes with electric stoves. On expansion of the cohort, however, the reductions in FEV_1 and FVC, although still statistically significant, were 0.6% of predicted for the former and 0.7% for the latter (92). With adjustment for parental education, the effects of exposure to a gas stove were reduced by 30% and were no longer statistically significant. Cross-sectional analysis of lung function data collected at the children's second examination did not show significant effects of stove type. With extension of the follow-up interval, the investigators assessed determinants of pulmonary function growth and found no effect of gas stove exposure (114).

Hasselbad and associates (192) analyzed data from the Environmental Protection Agency's Community Health Environmental Surveillance System. They reported that in girls 9 to 13 yr of age, gas stove exposure decreased $FEV_{0.75}$ by an average of 18 ml after adjustment for parental education level and smoking status. An effect was not observed in girls 6 to 8 yr of age nor in boys 6 to 13 yr of age.

In another large cross-sectional study, Vedal and colleagues (193) examined the effects of stove type on spirometric volumes and flow rates in a sample of 3,175 children ages five to 14 years. With adjustment for parental smoking and socioeconomic status, exposure to a gas stove was not significantly associated with reduced lung function level.

The effects of gas stove exposure on lung function level were assessed in 5 other investigations, but the sample sizes were inadequate for detecting effects of the magnitude found in the larger studies. Keller and colleagues (184) performed spirometry on 1 occasion in a sample of the subjects in their surveillance study. The data were not reported separately for children, and overall there was no effect of stove type. In 1 of the cross-sectional surveys conducted in England, the investigators correlated lung function level with 1-wk measurements of NO_2 in the kitchen and in the childrens' bedrooms (180). With a sample of about 400 children, significant effects of NO_2 were not found. Dodge (188) and Ekwo and associates (91) did not find effects of stove type on lung function measures in their cross-sectional studies. Hosein and Corey (110) examined the influence of 9 indoor factors on $FEV_{1.0}$ in 1,357 nonsmoking white children from 3 U.S. towns. They preliminarily reported that exposure to gas stoves was significantly associated with a 0.148-L reduction in FEV_1 level in boys and 0.75-L in girls.

Only a few investigations provide data on acute and chronic effects of NO_2 exposure indoors on adults (table 8). Prospective studies of acute respiratory illness occurrence have not demonstrated excesses in residents of homes with gas stoves (184, 185, 197). Cigarette smoking and chronic respiratory diseases, potential confounding variables, were not considered in these studies.

Potential chronic effects have also been examined in populations of adults (table 8). Comstock and coworkers (195) reported that gas stove use was associated with a significantly increased prevalence of certain chronic respiratory symptoms and of ventilatory impairment in nonsmoking men, but not in smoking men or in women of either smoking status. A subsequent reanalysis limited to the never and former smokers showed significant increases in chronic cough and phlegm and in the prevalence of low FEV_1/FVC in association with gas stove use in both sexes (196).

In a study of 97 nonsmoking rural women from the Netherlands, personal exposure estimates were created by combining 1-wk measurements of NO_2 with time-activity information (118). The investigators demonstrated a cross-sectional association between lung function level and current NO_2 exposure but failed to show an association between retrospectively estimated exposure to NO_2 and longitudinal decline in pulmonary function during the antecedent 17 yr (194).

Using a case-control design, Jones and associates (121) compared cooking fuel exposures of 20- to 39-yr-old nonsmoking women in the highest and lowest quartiles of the lung function distribution in the Tecumseh Community Health Study. The odds ratio for the effect of cooking with gas on lung function level was 1.82 (p = 0.076).

Lebowitz and colleagues (124, 198, 199) have evaluated acute effects of gas stove exposure on lung function and symptoms

in 229 subjects drawn from 117 Tucson households. The families were sampled from a larger study population to include persons with and without asthma, allergies, and airway obstruction. During a 2-yr period, subjects completed symptom diaries and monitored their peak flow daily. Multivariate analyses indicated adverse effects of gas stoves on symptoms and peak flow rate in asthmatics but not in normal subjects (199). However, the magnitude of the effect is difficult to determine from the available publications.

Recently, Kasuga (200) proposed that the urinary hydroxyproline to creatinine ratio is a valid and sensitive indicator of lung damage from environmental pollutants, including tobacco smoke and NO_2. Hydroxyproline, an amino acid constituent of collagen, is a product of collagen catabolism; therefore, an increase in its excretion reflects an increase in collagen destruction.

Matsuki and associates (115, 201) conducted a cross-sectional study of 820 schoolchildren and their 546 mothers during both a summer and a winter period. They measured subjects' 24-h personal NO_2 exposures with filter badges and collected early morning urine samples for evaluation of the hydroxyproline to creatinine ratio. In multiple regression equations, passive smoking status and personal NO_2 were independent and significant predictors of this ratio in both schoolchildren and adult women in both seasons. Distance from a main road, as a surrogate for exposure to automobile exhaust, was found to be a stronger predictor of the ratio in summer than in winter in schoolchildren and a predictor only during the summer in adult women. A linear relationship was also found between the value of the ratio and the amount of passive exposure to tobacco smoke. Other studies, however, have not shown relationships of the hydroxyproline to creatinine ratio with either passive exposure to tobacco smoke (116) or with active smoking (117). Although the hydroxyproline to creatinine ratio could serve as a useful biochemical indicator of lung injury by NO_2 exposure, further investigations are needed to clarify ambiguities in the available data.

Definitive statements concerning the risk of NO_2 exposure from cooking with gas stoves cannot be made at present. Although many studies have examined respiratory illnesses, respiratory symptoms, and lung function in children and adults, their results are not consistent and are not adequate for establishing a causal relationship. Retrospective illness histories may be inaccurate and their results biased by whether the subjects have symptoms or illness at the time of interview (93). Variations in the characteristics of the study populations and differing endpoints may partly explain the differences among the studies. Confidence limits have not been uniformly presented in the studies on gas stoves, and the results of many of the smaller studies that have been judged as negative are probably consistent with the larger studies that show small effects.

Unfortunately, NO_2 exposures were directly measured in only a few investigations (180, 181, 191, 194), and in all of these the measurements spanned at most 2-wk periods. In the other studies, categorical variables, indicating gas or electric stove use, were employed. However, neither limited area measurements nor variables for stove type tightly predict actual personal exposure (170). Thus, the results of all investigations of the health effects of NO_2 exposure from gas stoves are affected by random misclassification. This type of bias reduces the magnitude of the observed association from the value that would be found if the exposure of subjects was correctly estimated (25). Ozkaynak and associates (202) have shown that misclassification introduced by the use of a categorical variable for stove type may introduce substantial underestimation of the true relative risk values associated with the actual NO_2 exposure.

Bias from inadequate control of confounding factors must also be considered in interpreting the foregoing studies (203). Confounding occurs when the effect of 1 variable on the outcome of interest has not been separated from the effects of other variables. For example, maternal smoking has been associated with reduced lung function level in children. Confounding by maternal smoking could arise in a particular study if mothers of infants living in homes with gas stoves were more likely to smoke. With regard to NO_2 exposure from gas stoves and effects on respiratory illnesses and symptoms, and pulmonary function in children, the potential confounding variables include parental smoking, socioeconomic status, and asthma. Active smoking, occupational exposures, and the presence of chronic respiratory diseases should also be considered in adults. Control of these potentially confounding factors has been variable among published studies (203), and in some studies socioeconomic status has been treated as a confounding factor. However, the effect of socioeconomic status represents a summation of the effects of associated environmental and familial factors, one of which may be gas stove exposure. Thus, control for socioeconomic status may reduce the likelihood of finding an effect of gas stove exposure.

Summary. The findings on NO_2 exposure and respiratory illnesses indicate that the magnitude of the NO_2 effect at concentrations encountered in most U.S. homes is likely to be small. Groups with particularly high exposures, such as the urban poor who heat with ovens and those who heat their homes with kerosene or gas space heaters, have not yet been adequately investigated. The evidence on respiratory symptoms and lung function level in children and adults is also inconclusive. However, because more than half of U.S. homes have gas cooking stoves and childhood respiratory illness is extremely common, even a small effect of gas stoves would assume public health importance. In order to detect associations of the anticipated small magnitude, future investigations should employ direct measurement of exposure, rather than surrogate variables. Infants and other potentially susceptible groups seem the most suitable populations for study. Nevertheless, the epidemiologic evidence implies that clinically relevant effects of NO_2 from gas stoves are uncommon at the concentrations found in most U.S. homes.

Carbon Monoxide

Introduction. Carbon monoxide is an odorless, colorless gas with well-characterized effects on oxygen transport (204). Carbon monoxide interferes with oxygen transport by avidly binding to hemoglobin to form carboxyhemoglobin and by shifting the oxyhemoglobin dissociation curve to the left. It also binds to myoglobin, but the physiologic significance of the formation of CO-myoglobin has not been established (205). Carboxyhemoglobin reduces oxygen delivery to tissues, as does the hypoxia of altitude. Tissues with the highest oxygen needs, myocardium, brain, and exercising muscle, are most affected by the formation of carboxyhemoglobin. Research on the health effects of lower levels of carbon monoxide exposure has emphasized consequences for these organs, particularly in subjects with diseases that make these organs vulnerable to reduced oxygen transport.

Exposure. Carbon monoxide has numerous sources in the home, the office, and other environments. In the home, emissions from gas appliances and cigarette

smoke, and from vehicles in attached garages may elevate CO levels. During cooking with a gas range, hourly CO concentrations typically range from 2 to 6 ppm and 1-h averages may exceed 12 ppm in conventional homes (28). One-hour CO concentrations in small apartments may reach twice the values in single-family residences. Use of gas stove for heating, a common practice among urban poor in northern climates, may increase CO concentrations to 25 to 50 ppm (206). Cigarette smoking is generally a minor source of CO in homes (64). Other combustion sources in homes are kerosene and gas space heaters (207–209).

Carbon monoxide exposure may also be received in vehicles, particularly when entry routes are available for CO from exhaust (210). During urban commuting, CO levels in cars may average 2 to 5 times the concentrations generally measured in homes and offices and by ambient air monitors (211–213). Offices may be contaminated by vehicle exhaust because of building design problems; high CO levels may result (214).

Health Effects. Most evidence on the health effects of low levels of exposure to carbon monoxide, as generally encountered in indoor environments, has been derived from experimental human exposures. This line of investigation has emphasized disease states that increase susceptibility to reductions of oxygen transport: coronary artery disease, peripheral vascular disease, and chronic obstructive pulmonary disease (204, 215, 216). While the evidence was once considered to indicate adverse effects of CO at low levels in affected persons, much of the data is now controversial.

Although the health effects of low levels of CO exposure are controversial, the problem of CO poisoning by indoor combustion sources has been well described and its dimensions should be recognized by clinicians. The clinical manifestations of CO poisoning primarily reflect the effects of reduced oxygen transport to organs, such as the heart and brain, with high oxygen demand. The neurologic manifestations range from impaired mentation and behavioral alterations to coma (217, 218). Delayed and persistent neurologic sequelae may follow CO poisoning (218). Cardiac effects include arrhythmias and myocardial infarction (217).

The nonspecificity and diversity of the manifestations of CO poisoning have been emphasized (217). In fact, the diagnosis of CO poisoning is frequently delayed while alternative diagnoses are considered. In a series from France, the most common misdiagnoses were food poisoning, psychiatric disorders, cerebrovascular disease, intoxication, and heart disease (219). The finding of retinal hemorrhages on fundoscopic examination should alert the clinician to possible CO poisoning (220, 221). Kelly and Sophocleus (220) reported 12 cases of subacute CO poisoning; retinal hemorrhages were found in each of the 5 patients exposed more than 12 h. The incidence of CO poisoning may rise with increased use of space heaters and woodstoves.

Summary. Carbon monoxide poisoning is a well-documented clinical entity that follows exposure to high levels of CO. Effects of the lower levels of CO exposure generally encountered in indoor environments are controversial at present.

Woodsmoke

Introduction. Since the 1973 oil embargo, there has been a resurgence of residential wood use in the United States. During the decade of the 1970s, the shipment of woodstoves increased 10-fold and the current inventory of woodstoves is estimated to exceed 11 million (222). Residential woodburning typically occurs under oxygen-starved conditions that increase emission rates for CO, respirable particulates, and polycyclic aromatic hydrocarbons. In many communities where woodburning is common, ambient concentrations of these pollutants have increased as a result (223). The use of fireplaces and stoves may potentially result in increased indoor concentrations of smoke components by reentrainment of outdoor air or by direct leakage into indoor air.

Exposure. Few assessments of the impact of woodburning stoves and fireplaces on indoor air quality have been performed. Limited evidence suggests that the rate of pollutant emissions from a wood-burning source depends primarily on the degree of air-tightness of the source. Under proper operating conditions the newer "airtight" residential woodstove is under negative pressure and should not leak combustion by-products into the home. However, under non-airtight operations and during startup, stoking, and reloading, pollutants can be emitted indoors. Traynor and colleagues (224) reported indoor CO concentrations of 0.4 to 2.8 ppm during operation of "airtight" stoves, whereas average levels of 1.8 to 14 ppm occurred during operation of "non-airtight" stoves. For submicron sized particles, indoor concentrations were slightly above background (zero to 30 $\mu g/m^3$) during the use of "airtight" stoves and substantially higher with the "non-airtight" stoves (200 to 1,900 $\mu g/m^3$). Indoor concentrations of 5 polycyclic aromatic hydrocarbons greatly exceeded outdoor levels when the "non-airtight" stove was used (224).

These results are consistent with the findings of a study of personal exposures to respirable particulates in a rural community with substantial woodburning for winter heating (225). Analysis of respirable particulate data collected over 7 days of sampling in 24 homes in Waterbury, Vermont, suggested that homes with airtight woodburning stoves have about 4 $\mu g/m^3$ higher indoor concentrations than do the homes without woodburning stoves (225). The elemental composition of indoor and outdoor particles was examined for 5 of these homes. Using the elements as tracers for wood, automobile exhaust, and other sources of particles, as well as for measuring penetration of ambient air, the investigators confirmed that the increased indoor particle levels were due to woodburning.

Elevated concentrations of pollutants may also be caused by woodburning in fireplaces. Moschandreas and colleagues (63, 226) reported benzo(a)pyrene and respirable particulate levels indoors and outdoors from a series of measurements made in 3 homes, 2 with fireplaces and the third with a woodstove. The outdoor concentrations of benzo(a)pyrene rarely exceeded 1 ng/m^3. The indoor benzo(a)pyrene concentrations were substantially higher than outdoors on days when the woodstove was used, averaging 4.7 ng/m^3 indoors. Benzo(a)pyrene was only measured on 1 woodburning day for 1 home with a fireplace. On this day, the integrated particle samples indoors exceeded 11 ng/m^3 benzo(a)pyrene, while those outdoors were less than 0.5 ng/m^3. Respirable particulates were also elevated in all 3 residences on woodburning days. Levels ranged from 14.3 to 72.5 $\mu g/m^3$ in the home with the woodstove, and were 159.9 and 67.6 $\mu g/m^3$ on 1 woodburning day in each of the homes with a fireplace. The investigators concluded that woodburning in a stove or a fireplace may be an important source of indoor pollution.

In summary, airtight woodstoves contribute relatively low concentrations of particulates, CO, and polyaromatic hydrocarbons to the indoor environment. Woodburning in fireplaces and non-

airtight woodstoves may lead to substantially higher levels of these pollutants. Nonetheless, woodsmoke is a complex mixture and only a few of its components have been measured in homes. For example, measurements of aldehydes such as acroleiń have not been performed during residential woodburning. However, the characteristic smell of woodburning in stoves and fireplaces indicates that odorous compounds, some of which are most likely aldehydes, are released by combustion of wood. Further assessment of the impact of woodburning on indoor air quality is needed to describe fully the range of contaminants produced and their concentrations under differing conditions of operation and combustion.

Health Effects. Limited data have been published concerning the health effects of residential wood combustion. *In vitro* experiments demonstrate that emissions from a woodstove induce sister chromatid exchange (227) and are mutagenic, as assessed by the Ames Salmonella assay (228). Using a rabbit model, Fick and colleagues (229) studied the effects of woodsmoke on pulmonary macrophages. They reported that smoke-exposed rabbits, in comparison with controls, produced significantly more cells of all types on bronchoalveolar lavage, and that the rabbit macrophages exhibited a decrease in adherence, phagocytic rate and bacterial uptake. Macrophage viability and bactericidal processing were not affected. Wong and coworkers (230) evaluated the response of guinea pigs to woodsmoke with repeated CO_2 challenges. After exposure, respiratory frequency decreased and ventilatory response to CO_2 was diminished. These effects were transient and full recovery occurred within 3 days.

Only a few epidemiologic studies on the health effects of woodsmoke have been performed. Studies from less developed countries indicate an association between intense smoke exposure in dwellings and chronic pulmonary disease. In a house-to-house survey of adults more than 20 yr of age in Nepal, Pandey (231) found that chronic bronchitis was equally prevalent in men and women, affecting 18.9%, in contrast to the male preponderance usually observed. Further analysis of the data demonstrated an association between prevalence rates for chronic bronchitis and domestic smoke exposure as measured by the number of hours spent daily near the stove (232). Pandey and colleagues (233) subsequently evaluated respiratory function of 150 women ages 30 to 44 yr from 2 rural villages in Nepal. In cigarette smokers, spirometric test results worsened as reported hours of smoke exposure increased, but a similar effect was not present in nonsmokers.

Master (234) randomly selected 94 New Guinea residents for a health evaluation that included a complete history and physical examination. The prevalence of clinical symptoms or abnormal pulmonary findings was extremely high at all ages; 90% of subjects 40 yr of age and older were affected. Although Master collected only descriptive clinical data and no information on exposures, he attributed the high prevalence of abnormalities to domestic smoke exposure. Based on the findings of a cross-sectional study, Anderson (235) has also suggested that woodsmoke exposure contributes to the development of chronic lung disease in adults in New Guinea.

Respiratory effects of woodsmoke have also been examined in children from less developed countries. Anderson (236) conducted a cross-sectional study and a longitudinal study to assess the effects of woodsmoke pollution on children in New Guinea. He evaluated 1,650 children drawn from 2 contrasting communities, 1 at sea level where wood was not burned and 1 in the highlands where wood was commonly burned. The 2 groups did not differ on spirometric testing, physical examination, or clinical history. He also followed 112 children with differing levels of woodsmoke exposure and did not find a consistent relationship between exposure and respiratory abnormalities during a 30-wk surveillance period. In contrast, Kossove (237) reported that Zulu infants less than 13 months of age with severe lower respiratory tract diseases were twice as likely to have a history of daily heavy smoke exposure as were infants without such disease.

Although these studies implicate domestic smoke exposure as a risk factor for the development of respiratory disease in less developed nations, their results should not be generalized to more developed nations. The exposures are orders of magnitude lower on average in more developed countries than in less developed countries. In the less developed countries, low efficiency stoves are used for long periods of time in small huts with poor ventilation, and agricultural waste and dung are often used as fuel (238). These conditions may lead to particulate and benzo(a)pyrene levels that are 10 to 100 times higher than those found in U.S. homes with woodburning stoves (239).

Data on health effects of residential wood combustion in the United States are sparse. In a case report, Honicky and colleagues (240) described an infant with recurrent hospitalizations for severe lower respiratory tract disease characterized by wheeze and pneumonia. The child improved when hospitalized and then relapsed within 12 h after returning home. After the parents removed their woodstove, the child's illnesses ceased. This case prompted the investigators to conduct a prevalence study of respiratory symptoms in 62 children in Michigan, 31 from homes with and 31 from homes without woodburning stoves (241). Using a standardized questionnaire, interviewers asked parents about their children's respiratory symptoms during the previous winter. Symptoms were classified as present or absent and as mild, moderate, or severe. The proportion of children with moderate or severe symptoms was much greater in the group from homes with woodstoves: 84% of children in this group reported at least 1 severe symptom as compared to 3% of the control group. Parental smoking and socioeconomic status were similar in both groups.

In a study of similar design in Massachusetts, Tuthill (242) retrospectively ascertained episodes of acute respiratory illnesses from January through March from 399 parents of school-age children. In contrast to Honicky's results, use of a woodburning stove was not associated with chronic respiratory disease, symptoms such as fever, sore throat, rhinitis, cough and wheeze, or excess (more than 1) respiratory illness. Differences in study populations, type of wood burned or ascertainment of illness may explain the conflicting results of these studies.

Another potential hazard of woodburning stoves is illustrated by a recent case report of a Wisconsin family that experienced arsenic poisoning (243). Over a 3-yr period, the family displayed a variety of symptoms ranging from rashes and muscle cramps to seizures and loss of consciousness. An environmental evaluation of their house revealed that they were burning plywood treated with a chromium-copper-arsenate mixture in their stove.

Summary. Woodsmoke is a complex mixture of gases and particles that has a wide range of potential respiratory effects. The unconfirmed observations of Honicky and colleagues (241) that woodsmoke causes acute respiratory illnesses and symptoms in U.S. children require further study. Investigations in less developed countries suggest that domestic

smoke exposure contributes to the development of chronic lung disease. This important hypothesis cannot be tested with sufficient sensitivity in most populations in the United States but should be pursued in appropriate locales. Recurrent severe respiratory disease with no underlying causes in an infant should prompt the clinician to determine whether a woodstove is present in the home. In these situations, a therapeutic trial of discontinuing its use seems warranted.

Addendum

During 1987, several new sources of information on indoor air pollution and health have been published. The 4th International Conference on Indoor Air Quality and Climate was held in August 1987. The proceedings were published by the Institute for Water, Soil and Air Hygiene in Berlin (mailing address: Institut für Wasser-, Boden- und Lufthygiene des Bundesgesundheitsamtes, Corrensplatz 1, D-1000 Berlin 33). The U.S. Environmental Protection Agency report "EPA Indoor Air Quality Implementation Plan" and its appendices provide a comprehensive review. Two new reports on environmental radon are available: "Lung Cancer Risk from Indoor Exposure to Radon Daughters," Publication 50 of The International Commission on Radiological Protection, and the report of the Biological Effects of Ionizing Radiation (BEIR) IV Alpha Committee of the National Academy of Sciences.

References

1. Szalai A, ed. The use of time: daily activities of urban and suburban populations in twelve countries. The Hague: Mouton, 1972.

2. Chapin FS Jr. Human activity patterns in the city. New York: A Wiley-Interscience Publication, 1974.

3. Benson FB, Henderson JJ, Caldwell DE. Indoor-outdoor air pollution relationships: a literature review. Research Triangle Park, NC: U.S. Environmental Protection Agency, 1972. Publication No. AP-112.

4. Henderson JJ, Benson FB, Caldwell DE. Indoor-outdoor air pollution relationships: Vol. 2. An annotated bibliography. Research Triangle Park, NC: U.S. Environmental Protection Agency, 1973. Publication No. AB-112B.

5. Sexton K. Indoor air quality: an overview of policy and regulatory issues. Sci Technol Human Values 1986; 11:53–67.

6. Environmental Protection Agency. National air quality and emissions trends report, 1981. Research Triangle Park, NC: Environmental Protection Agency, 1983. EPA-450/4-83-011.

7. Boleij JS, Brunekreef B. Indoor air pollution. Public Health Rev 1982; 10:169–98.

8. Repace JL. Indoor air pollution. Environ Int 1982; 8:21–36.

9. Lebowitz MD. Health effects of indoor pollutants. Annu Rev Public Health 1983; 4:203–21.

10. Spengler JD, Sexton K. Indoor air pollution: a public health perspective. Science 1983; 221:9–17.

11. Meyer B. Indoor air quality. Reading, MA: Addison-Wesley Publishing Co., Inc., 1983.

12. Wadden RA, Schiff PA. Indoor air pollution: characterization, prediction, and control. New York: Wiley, 1983.

13. Turiel I. Indoor air quality and human health. Stanford, CA: Stanford University Press, 1985.

14. Walsh PJ, Dudney CS, Copenhaver ED, eds. Indoor air quality. Boca Raton, FL: CRC Press, Inc., 1984.

15. National Research Council, Committee on Indoor Pollutants. Indoor pollutants. Washington, D.C.: National Academy Press, 1981.

16. Symposium and health aspects of indoor air pollution. Bull NY Acad Med 1981; 57:825–1084.

17. Spengler J, Hollowell C, Moschandreas D, Fanger O, eds. Indoor air pollution: a special issue of *Environment International*. Environ Int 1982; 8:1–534.

18. International symposium on effects of indoor air pollution with special reference to nitrogen oxides and smoking. Tokai J Exp Clin Med 1985; 10:253–486.

19. Berglund B, Lindvall T, Sundell J, eds. Indoor air. Vol. 1. Recent advances in the health sciences and technology. Stockholm: Swedish Council for Building Research, 1984.

20. Berglund B, Lindvall T, Sundell J, eds. Indoor air. Vol. 2. Radon, passive smoking, particulates and housing epidemiology. Stockholm: Swedish Council for Building Research, 1984.

21. Berglund B, Lindvall T, Sundell J, eds. Indoor air. Vol. 3. Sensory and hyperreactivity reactions to sick buildings. Stockholm: Swedish Council for Building Research, 1984.

22. Berglund B, Lindvall T, Sundell J, eds. Indoor air. Vol. 4. Chemical characterization and personal exposure. Stockholm: Swedish Council for Building Research, 1984.

23. Berglund B, Lindvall T, Sundell J. Indoor air. Vol. 5. Buildings, ventilation and thermal climate. Stockholm: Swedish Council for Building Research, 1984.

24. Gammage RB, Kaye SV, eds. Indoor air and human health. Chelsea, MI: Lewis Publishers, 1985.

25. Shy CM, Goldsmith JR, Hackney JD, Lebowitz MD, Menzel DB. Health effects of air pollution. ATS News 1978; 6:1–63.

26. Yocom J. Indoor-outdoor air quality relationships: a critical review. J Air Pollut Control Assoc 1982; 32:500–20.

27. National Research Council, Committee on the Epidemiology of Air Pollutants. Epidemiology and air pollution. Washington, D.C.: National Academy Press, 1985.

28. Moschandreas DJ, Stark JWC, McFadden JE, Morse SS. Indoor air pollution within residential environments. Vols. 1 & 2. Washington D.C.: U.S. Environmental Protection Agency, 1978. USEPA 600/7-78-223.

29. Lebowitz MD, Corman G, O'Rourke MK, Holberg CJ. Indoor-outdoor air pollution, allergen and meterological monitoring in an arid southwest area. J Air Pollut Control Assoc 1984; 34:1035–8.

30. National Research Council, Committee on Airliner Cabin Air Quality. The airliner cabin environment: air quality and safety. Washington, D.C.: National Academy Press, 1986.

31. Elliot LP, Rowe DR. Air quality during public gatherings. J Air Pollut Control Assoc 1975; 25:635–6.

32. Spengler JD, Stone KR, Lilley FW. High carbon monoxide exposures in enclosed skating rinks. J Air Pollut Control Assoc 1978; 28:776–9.

33. Wallace LA. An overview of the total exposure assessment methodology (team) study. Final report. Washington, D.C.: U.S. Environmental Protection Agency, 1986.

34. Spengler JD, Cohen MA. Emissions from indoor combustion sources. In: Gammage RB, Kaye SV, eds. Indoor air and human health. Chelsea, MI: Lewis Publishers, 1985; 261–78.

35. Henderson Y, Turner JM, Carbon monoxide as a hazard of polar exploration. Nature 1940; 145:92–5.

36. Pugh LGCE. Carbon monoxide hazard in Antarctica. Br Med J 1959; 1:192–6.

37. Spengler JD, Soczek ML. Evidence for improved ambient air quality and the need for personal exposure research. Environ Sci Technol 1984; 18:268–80.

38. Wallace LA, Ott WR. Personal monitors: a state-of-the-art survey. J Air Pollut Control Assoc 1982; 32:601–10.

39. Rose VE, Perkins JL. Passive dosimetry—state of the art review. Am Ind Hyg Assoc J 1982; 43:605–21.

40. Spengler JD, Treitman RD, Tosteson TD, Mage DT, Soczek ML. Personal exposures to respirable particulates and implications for air pollution epidemiology. Environ Sci Technol 1985; 19:700–7.

41. Quackenboss JJ, Kanarek MS, Spengler JD, Letz R. Personal monitoring for nitrogen dioxide exposure: methodological considerations for a community study. Environ Int 1982; 8:249–58.

42. National Research Council, Committee on Nonoccupational Health Risks of Asbestiform Fibers. Asbestiform fibers: nonoccupational health risks. Washington, D.C.: National Academy Press, 1984.

43. U.S. Department of Health, Education, and Welfare, Public Health Service. Smoking and health. A report of the surgeon general. Washington, D.C.: U.S. Government Printing Office, 1979. DHEW (PHS) 79-50066.

44. First MW. Constituents of sidestream and mainstream tobacco and markers to quantify exposure to them. In: Gammage RB, Kaye SV, eds. Indoor air and human health. Chelsea, MI: Lewis Publishers, 1985; 195–203.

45. U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health. The health consequences of smoking: chronic obstructive lung disease. A report of the surgeon general. Washington, D.C.: U.S. Government Printing Office, 1984. DHHS (PHS) 84-50205.

46. U.S. Department of Health and Human Services. Public Health Service, Office on Smoking and Health. The health consequences of involuntary smoking. A report of the surgeon general. Washington, D.C.: U.S. Government Printing Office, 1986.

47. National Research Council, Committee on Passive Smoking. Environmental tobacco smoke: measuring exposures and assessing health effects. Washington, D.C.: National Academy Press, 1986.

48. Sterling TD, Kobayashi D. Indoor byproduct levels of tobacco smoke: a critical review of the literature. J Air Pollut Control Assoc 1982; 32: 250–9.

49. Everson RB, Sandler DP, Wilcox AJ, Schreinemachers D, Shore DL, Weinberg C. Effect of passive exposure to smoking on age at natural menopause. Br Med J 1986; 293:792.

50. Toubas PL, Duke JC, McCaffree MA, Mattice CD, Bendell D, Orr WC. Effects of maternal smoking and caffeine habits on infantile apnea: a retrospective study. Pediatrics 1986; 78:159–63.

51. Martin TR, Bracken MD. Association of low birth weight with passive smoke exposure in pregnancy. Am J Epidemiol 1986; 124:633–42.

52. Rubin DH, Leventhal JM, Krasilnikoff PA, Weile B, Berget A. Effect of passive smoking on birth-weight. Lancet 1986; 2:415–7.

53. Weiss ST, Tager IB, Schenker M, Speizer FE. The health effects of involuntary smoking. Am Rev Respir Dis 1983; 128:933–42.

54. Rylander R, Peterson Y, Snella MC, eds. ETS—Environmental tobacco smoke. Report from a workshop on the effects and exposure levels, March 15–17, 1983, Geneva, Switzerland. Eur J Respir Dis 1984; 65(Suppl 133:5–152).

55. Proceedings of the international symposium on medical perspectives on passive smoking, Vienna, 1984. Prev Med 1984; 13:557–746.

56. Shephard RJ. The risks of passive smoking. New York: Oxford University Press, 1982.

57. Lefcoe NM, Ashley MJ, Pederson LL, Keays JJ. The health risks of passive smoking: the growing case for control measures in enclosed environments. Chest 1983; 84:90–5.

58. Samet JM, Speizer FE. Passive smoking and the lungs: a review of effects other than malignancy. In: Forbes WF, Frecker RC, Nostbakken D, eds. Proceedings of the Fifth World Congress on Smoking and Health, Winnipeg. Vol. 1. Ottawa: Canadian Council on Smoking and Health, 1983; 199–205.

59. Guyatt GH, Newhouse MT. Are active and passive smoking harmful? Determining causation. Chest 1985; 88:445–51.

60. Samet JM. Relationship between passive exposure to cigarette smoke and cancer. In: Gammage RB, Kaye SV, eds. Indoor air and human health. Chelsea, MI: Lewis Publishers, 1985; 227–40.

61. Higgins M. Critical review of the relationship between passive exposure to cigarette smoke and cardiopulmonary disease. In: Gammage RB, Kaye SV, eds. Indoor air and human health. Chelsea, MI: Lewis Publishers, 1985; 241–56.

62. Spengler JD, Dockery DW, Turner WA, Wolfson JM, Ferris BG Jr. Long-term measurements of respirable sulfates and particles inside and outside homes. Atmos Environ 1981; 15:23–30.

63. Moschandreas JD, Zabransky J, Peltas DJ. Comparison of indoor and outdoor air quality. Menlo Park, CA: Electric Power Research Institute (Report EA-1733), 1981.

64. Brookman, ET, Birenzvigi A. Exposure to pollutants from domestic combustion sources: a preliminary assessment. Wethersfield, CT: TRC Environmental Consultants, Inc., 1981. NTIS Report PB81-111536.

65. Repace JL, Lowrey AH. Indoor air pollution, tobacco smoke, and public health. Science 1980; 208:464–72.

66. Jarvis MJ, Russell MA. Measurement and estimation of smoke dosage to non-smokers from environmental tobacco smoke. Eur J Respir Dis 1984; 65(Suppl 133:68–75).

67. Rosenberg J, Benowitz NL, Jacob P, Wilson KM. Disposition kinetics and effects of intravenous nicotine. Clin Pharmacol Ther 1980; 28:517–22.

68. Kyerematen GA, Damiano MD, Dvorchik BH, Vesell ES. Smoking-induced changes in nicotine disposition: application of a new HPLC assay for nicotine and its metabolites. Clin Pharmacol Ther 1982; 32:769–80.

69. Benowitz NL, Kuyt F, Jacob P III, Jones RT, Osman AL. Cotinine disposition and effects. Clin Pharmacol Ther 1983; 34:604–11.

70. Hoffman D, Brunneman KD, Adams JD, Haley NJ. Indoor air pollution by tobacco smoke: model studies on the uptake by nonsmokers. In: Berglund B, Lindvall T, Sundell J, eds. Indoor air. Vol. 2. Radon, passive smoking, particulates and housing epidemiology. Stockholm: Swedish Council for Building Research, 1984; 313–8.

71. Hoffman D, Haley NJ, Adams JD, Brunneman KD. Tobacco sidestream smoke: uptake by nonsmokers. Prev Med 1984; 13:608–17.

72. Jarvis M, Tunstall-Pedoe H, Feyerabend C, Vesey C, Salloojee Y. Biochemical markers of smoke absorption and self reported exposure to passive smoking. J Epidemiol Community Health 1984; 38:335–9.

73. Wald NJ, Boreham J, Bailey A, Ritchie C, Haddow JE, Knight G. Urinary cotinine as marker of breathing other people's tobacco smoke (letter). Lancet 1984; 1:230–1.

74. Wald N, Ritchie C. Validation of studies on lung cancer in non-smokers married to smokers (letter). Lancet 1984; 1:1067.

75. Greenberg RA, Haley NJ, Etzel RA, Loda FA. Measuring the exposure of infants to tobacco smoke: nicotine and cotinine in urine and saliva. N Engl J Med 1984; 310:1075–8.

76. Matsukura S, Taminato T, Kitano N, *et al*. Effects of environmental tobacco smoke on urinary cotinine excretion in nonsmokers: evidence for passive smoking. N Engl J Med 1984; 311:828–32.

77. Jarvis MJ, Russell MA, Feyerabend C, *et al*. Passive exposure to tobacco smoke: saliva cotinine concentrations in a representative population sample of non-smoking schoolchildren. Br Med J 1985; 291:927–9.

78. Pattishall EN, Strope GL, Etzel RA, Helms RW, Haley NJ, Denny FW. Serum cotinine as a measure of tobacco smoke exposure in children. Am J Dis Child 1985; 139:1101–4.

79. Coultas DB, Samet JM, Howard CA, Peake GT, Skipper BJ. Salivary cotinine levels and passive tobacco smoke exposure in the home (abstract). Am Rev Respir Dis 1986; 132(Suppl:A157–8).

80. Luck W, Nau H. Nicotine and cotinine concentrations in serum and urine of infants exposed via passive smoking or milk from smoking mothers. J Pediatr 1985; 107:816–20.

81. Poulton J, Rylance GW, Taylor AW, Edwards C. Serum thiocyanate levels as indicator of passive smoking in children (letter). Lancet 1984; 2:1405–6.

82. Bottoms SF, Kuhnert BR, Kuhnert PM, Reese AL. Maternal passive smoking and fetal serum thiocyanate levels. Am J Obstet Gynecol 1982; 144: 787–91.

83. Russell MA. Blood and urinary nicotine in non-smokers (letter). Lancet 1975; 1:179–81.

84. Feyerabend C, Higenbottam T, Russell MA. Nicotine concentrations in urine and saliva of smokers and nonsmokers. Br Med J 1982; 284: 1002–4.

85. Friedman GD, Petitti DB, Bawol RD. Prevalence and correlates of passive smoking. Am J Public Health 1983; 73:401–5.

86. Foliart D, Benowitz NL, Becker CE. Passive absorption of nicotine in flight attendants (letter). N Engl J Med 1983; 308:1105.

87. Russell MAH, West RJ, Jarvis MJ. Intravenous nicotine simulation of passive smoking to estimate dosage to exposed non-smokers. Br J Addict 1985; 80:201–6.

88. Pedreira FA, Guandolo VL, Feroli EF, Mella GW, Weiss IP. Involuntary smoking and incidence of respiratory illness during the first year of life. Pediatrics 1985; 75:594–7.

89. Yue C, Wanxian L, Shunzhang Y. Influence of passive smoking on admissions for respiratory illness in early childhood. Br Med J 1986; 293:303–6.

90. Wadsworth MEJ, Peckham CS, Taylor B. The role of national longitudinal studies in the prediction of health, development and behavior. In: Walker DK, Richmond JB, eds. Monitoring child health in the United States: selected issues and policies. Cambridge, MA: Harvard University Press, 1984; 63–83.

91. Ekwo EE, Weinberger MW, Lachenbruch PA, Huntley WH. Relationship of parental smoking and gas cooking to respiratory disease in children. Chest 1983; 84:662–8.

92. Ware JH, Dockery DW, Spiro A III, Speizer FE, Ferris BG Jr. Passive smoking, gas cooking, and respiratory health of children living in six cities. Am Rev Respir Dis 1984; 129:366–74.

93. Samet JM, Tager IB, Speizer FE. The relationship between respiratory illness in childhood and chronic air-flow obstruction in adulthood. Am Rev Respir Dis 1983; 127:508–23.

94. Gardner G, Frank AL, Taber LH. Effects of social and family factors on viral respiratory infection and illness in the first year of life. J Epidemiol Community Health 1984; 38:42–8.

95. Vogt TM. Effects of parental smoking on medical care utilization by children. Am J Public Health 1984; 74:30–4.

96. Pukander J, Luotonen J, Timonen M, Karmer P. Risk factors affecting the occurrence of acute otitis media among 2–3-year-old urban children. Acta Otolaryngol 1985; 100:260–5.

97. Kraemer JM, Richardson MA, Weiss NS, *et al*. Risk factors for persistent middle-ear effusions: otitis media, catarrh, cigarette exposure, and atopy. JAMA 1983; 249:1022–5.

98. Black N. The aetiology of glue ear—a case-control study. Int J Pediatr Otorhinolaryngol 1985; 9:121–33.

99. Iversen M, Birch L, Lundqvist GR, Elbrond O. Middle ear effusion in children and the indoor environment: an epidemiological study. Arch Environ Health 1985; 40:74–9.

100. Burchfiel CM 3d. Passive smoking, respiratory symptoms, lung function and initiation of smoking in Tecumseh, Michigan. Ann Arbor, MI: University of Michigan, Unpublished Ph.D. dissertation, 1984.

101. Burchfiel CM, Higgins MW, Keller JB, Howatt WF, Butler WJ, Higgins IT. Passive smoking in childhood. Respiratory conditions and pulmonary function in Tecumseh, Michigan. Am Rev Respir Dis 1986; 133:966–73.

102. Charlton A. Children's coughs related to parental smoking. Br Med J 1984; 288:1647–9.

103. McConnochie KM, Roghmann KJ. Predicting clinically significant lower respiratory tract illness in childhood following mild bronchiolitis. Am J Dis Child 1985; 139:625–31.

104. McConnochie KM, Roghmann KJ. Breast feeding and maternal smoking as predictors of wheezing in children age 6 to 10 years. Pediatr Pulmonol 1986; 2:260–8.

105. Murray AB, Morrison BJ. The effect of cig-

arette smoke from the mother on bronchial responsiveness and severity of symptoms in children with asthma. J Allergy Clin Immunol 1986; 77:575–81.

106. Tashkin DP, Clark VA, Simmons M, *et al.* The UCLA population studies of chronic obstructive respiratory disease. Relationship between parental smoking and children's lung function. Am Rev Respir Dis 1984; 129:891–7.

107. Horwood LJ, Fergusson DM, Shannon FT. Social and familial factors in the development of early childhood asthma. Pediatrics 1985; 75:859–68.

108. Weiss ST, Tager IB, Speizer FE, Rosner B. Persistent wheeze, its relation to respiratory illness, cigarette smoking, and level of pulmonary function in a population sample of children. Am Rev Respir Dis 1980; 122:697–707.

109. Weiss ST, Tager IB, Munoz A, Speizer FE. The relationship of respiratory infections in early childhood to the occurrence of increased levels of bronchial responsiveness and atopy. Am Rev Respir Dis 1985; 131:573–8.

110. Hosein R, Corey P. Multivariate analyses of nine indoor factors on FEV_1 of caucasian children (abstract). Am Rev Respir Dis 1984; 129(Suppl: A140).

111. Lebowitz MD, Knudson RJ, Burrows B. Family aggregation of pulmonary function measurements. Am Rev Respir Dis 1984; 129:8–11.

112. Tager IB, Weiss ST, Rosner B, Speizer FE. Effect of parental cigarette smoking on the pulmonary function of children. Am J Epidemiol 1979; 110:15–26.

113. Tager IB, Weiss ST, Munoz A, Rosner B, Speizer FE. Longitudinal study of the effects of maternal smoking on pulmonary function in children. N Engl J Med 1983; 309:699–703.

114. Berkey CS, Ware JH, Dockery DW, Ferris BG Jr. Indoor air pollution and pulmonary function growth in preadolescent children. Am J Epidemiol 1986; 123:250–60.

115. Matsuki H, Yanagisawa Y, Osaka F, Kasuga H, Nishimura H. Personal exposure to NO_2 and its health effect with urinary hydroxyproline to creatinine ratio as biochemical indicator. In: Berglund B, Lindvall T, Sundell J, eds. Indoor air. Vol. 2. Radon, passive smoking, particulates and housing epidemiology. Stockholm: Swedish Council for Building Research, 1984; 243–8.

116. Adlkofer F, Scherer G, Heller WD. Hydroxyproline excretion in urine of smokers and passive smokers. Prev Med 1984; 13:670–9.

117. Read GA, Thornton RE. Preliminary studies of urinary hydroxyproline levels in rodents and in smokers. Tokai J Exp Clin Med 1985; 10:445–50.

118. Remijn B, Fischer P, Brunekreef B, Levret E, Boleij JSM, Noij D. Indoor air pollution and its effect on pulmonary function of adult non-smoking women. I. Exposure estimates for nitrogen dioxide and passive smoking. Int J Epidemiol 1985; 14:215–20.

119. Brunekreef B, Fischer P, Remijn B, Van der Lende R, Schouten J, Quanjer P. Indoor air pollution and its effect on pulmonary function of adult non-smoking women: III. Passive Smoking and pulmonary function. Int J Epidemiol 1985; 14:227–30.

120. Gillis CR, Hole DJ, Hawthorne VM, Boyle P. The effect of environmental tobacco smoke in two urban communities in the west of Scotland. Eur J Respir Dis 1984; 65(Suppl 133:121–6).

121. Jones JR, Higgins IT, Higgins MW, Keller JB. Effects of cooking fuels on lung function in nonsmoking women. Arch Environ Health 1983; 38:219–22.

122. Kentner M, Triebig G, Weltle D. The influence of passive smoking on pulmonary function—a study of 1,351 office workers. Prev Med 1984; 13:656–69.

123. Lee PN, Chamberlain J, Alderson MR. Relationship of passive smoking to risk of lung cancer and other smoking-associated diseases. Br J Cancer 1986; 54:97–105.

124. Lebowitz MD. The effects of environmental tobacco smoke exposure and gas stoves on daily peak flow rates in asthmatic and non-asthmatic families. Eur J Respir Dis 1984; 65(Suppl 133:90–7).

125. Lebowitz MD. Influence of passive smoking on pulmonary function: a survey. Prev Med 1984; 13:645–55.

126. Wiedemann HP, Mahler DA, Loke J, Virgulto JA, Snyder P, Matthay RA. Acute effects of passive smoking on lung function and airway reactivity in asthmatic subjects. Chest 1986; 89:180–5.

127. U.S. Department of Health and Human Services, Public Health Service. Report on workshop on respiratory effects of involuntary smoke exposure: epidemiologic studies. Bethesda, MD: Public Health Service, National Institutes of Health, December, 1983.

128. Hirayama T. Non-smoking wives of heavy smokers have a higher risk of lung cancer: a study from Japan. Br Med J 1981; 282:183–5.

129. Trichopoulos D, Kalandidi A, Sparros L, MacMahon B. Lung cancer and passive smoking. Int J Cancer 1981; 27:1–4.

130. U.S. Department of Health and Human Services, Public Health Service. The health consequences of smoking: cancer. A report of the surgeon general. Washington, D.C.: U.S. Government Printing Office, 1982. DHHS (PHS) 82-50179.

131. Bos RP, Theuws JL, Henderson PT. Excretion of mutagens in human urine after passive smoking. Cancer Lett 1983; 19:85–90.

132. Sorsa M, Einisto P, Husgafvel-Pursiainen K, *et al.* Passive and active exposure to cigarette smoke in a smoking experiment. J Toxicol Environ Health 1985; 16:523–34.

133. Enstrom JE. Rising lung cancer mortality among nonsmokers. J Natl Cancer Inst 1979; 62:755–60.

134. Garfinkel L. Time trends in lung cancer mortality among nonsmokers and a note on passive smoking. J Natl Cancer Inst 1981; 66:1061–6.

135. Garfinkel L, Auerbach O, Joubert L. Involuntary smoking and lung cancer: a case-control study. J Natl Cancer Inst 1985; 75:463–9.

136. Hirayama T. Cancer mortality in nonsmoking women with smoking husbands based on a large-scale cohort study in Japan. Prev Med 1984; 13:680–90.

137. Chan WC, Colbourne MJ, Fung SC, Ho HC. Bronchial cancer in Hong Kong 1976–1977. Br J Cancer 1979; 39:182–92.

138. Chan WC. Lung cancer in non-smokers in Hong Kong. In: Grundmann E, ed. Cancer campaign. Vol. 6. Cancer epidemiology. Stuttgart: Gustav Fischer Verlag, 1982; 6:199–202.

139. Correa P, Pickle LW, Fontham E, Lin Y, Haenszel W. Passive smoking and lung cancer. Lancet 1983; 2:595–7.

140. Kabat GC, Wynder EL. Lung cancer in nonsmokers. Cancer 1984; 53:1214–21.

141. Koo LC, Ho JH, Lee N. An analysis of some risk factors for lung cancer in Hong Kong. Int J Cancer 1985; 35:149–55.

142. Koo LC, Ho JH-C, Saw D. Is passive smoking an added risk factor for lung cancer in Chinese women? J Exp Clin Cancer Res 1984; 3:277–83.

143. Wu AH, Henderson BE, Pike MC, Yu MC. Smoking and other risk factors for lung cancer in women. J Natl Cancer Inst 1985; 4:747–51.

144. Akiba S, Kato H, Blot WJ. Passive smoking and lung cancer among Japanese women. Cancer Res 1986; 46:4804–7.

145. Dalager NA, Pickle LW, Mason TJ, *et al.* The relation of passive smoking to lung cancer. Cancer Res 1986; 46:4808–11.

146. Humble CG, Samet JM, Pathak DR. Marriage to a smoker and lung cancer risk in New Mexico. Am J Public Health 1987; 77:598–602.

147. Hirayama T. Passive smoking and lung cancer: consistency of association (letter). Lancet 1983; 2:1425–6.

148. Trichopoulos D, Kalandidi A, Sparros L. Lung cancer and passive smoking: conclusion of Greek study (letter). Lancet 1983; 2:677–8.

149. Knoth A, Bohn H, Schmidt F. Passivrauchen als Lungenkrebsursache bei Nichtraucherinnen. Med Klin 1983; 2:66–9.

150. Repace JL. Consistency of research data on passive smoking and lung cancer (letter). Lancet 1984; 1:506.

151. U.S. Department of Health, Education, and Welfare, Public Health Service. Smoking and health. Report of the advisory committee to the surgeon general. Washington, D.C.: U.S. Government Printing Office, 1964. PHS Publication No. 1103.

152. World Health Organization, International Agency for Research on Cancer. IARC monographs on the evaluation of the carcinogenic risk of chemicals to humans: tobacco smoking, vol. 38. Lyon, France: IARC, 1986.

153. Weiss ST. Passive smoking and lung cancer. What is the risk? (Editorial). Am Rev Respir Dis 1986; 133:1–3.

154. Repace JL, Lowrey AH. A quantitative estimate of nonsmokers' lung cancer risk from passive smoking. Environ Int 1985; 11:3–22.

155. Preston-Martin S, Yu MC, Benton B, Henderson BE. N-nitroso compounds and childhood brain tumors: a case-control study. Cancer Res 1982; 42:5240–5.

156. Grufferman S, Wang HH, Delong ER, Kimm SY, Delzell ES, Falletta JM. Environmental factors in the etiology of rhabdomyosarcoma in childhood. J Natl Cancer Inst 1982; 68:107–13.

157. Everson RB. Individuals transplacentally exposed to maternal smoking may be at increased cancer risk in adult life. Lancet 1980; 2:123–7.

158. Grufferman S, Delzell ES, Maile MC, Michalopoulos G. Parents' cigarette smoking and childhood cancer. Med Hypotheses 1983; 12:17–20.

159. Miller GH. Cancer, passive smoking and nonemployed and employed wives. West J Med 1984; 140:632–5.

160. Sandler DP, Everson RB, Wilcox AJ. Passive smoking in adulthood and cancer risk. Am J Epidemiol 1985; 121:37–48.

161. Sandler DP, Everson RB, Wilcox AJ, Browder JP. Cancer risk in adulthood from early life exposure to parents' smoking. Am J Public Health 1985; 75:487–92.

162. Sandler DP, Wilcox AJ, Everson RB. Cumulative effects of lifetime passive smoking on cancer risk. Lancet 1985; 1:312–5.

163. Kabat GC, Dieck GS, Wynder EL. Bladder cancer in nonsmokers. Cancer 1986; 2:362–7.

164. U.S. Department of Health and Human Services, Public Health Service, Office on Smoking and Health. The health consequences of smoking. Cardiovascular Disease. A Report of the surgeon

general. Washington, D.C.: U.S. Government Printing Office, 1983. DHHS (PHS) 84-50204.

165. Hirayama T. Passive smoking and lung cancer, nasal sinus cancer, brain tumor and ischemic heart disease. In: Forbes WF, Frecker RC, Nostbakken eds. Proceedings of the Fifth World Conference on Smoking and Health, vol. 1. Ottawa: Canadian Council on Smoking and Health, 1983; 137-41.

166. Garland C, Barrett-Connor E, Suarez L, Criqui MH, Wingard DL. Effects of passive smoking on ischemic heart disease mortality of nonsmokers. Am J Epidemiol 1985; 121:645-50.

167. Vandenbroucke JP, Verheesen JH, De Bruin A, *et al.* Active and passive smoking in married couples: results of 25-year follow-up. Br Med J 1984; 288:1801-2.

168. Lowry T, Schuman LM. "Silo-filler's disease"—a syndrome caused by nitrogen dioxide. JAMA 1956; 162:153-60.

169. National Research Council, Committee on Medical and Biologic Effects of Environmental Pollutants, Subcommittee on Nitrogen Oxides. Nitrogen oxides. Washington, D.C.: National Academy of Sciences, 1976.

170. Spengler JD, Duffy CP, Letz R, Tibbitts TW, Ferris BG Jr. Nitrogen dioxide inside and outside 137 homes and implications for ambient air quality standards and health effects research. Environ Sci Technol 1983; 17:164-8.

171. U.S. Department of Commerce, Bureau of the Census. 1980 Census of housing. Vol. 1. Characteristics of housing units. Ch. B. Detailed housing characteristics. Pt. 1, United States summary. Washington, D.C.: U.S. Government Printing Office, 1983; T. 82 and T. 153. HC80-1-B1.

172. Sexton K, Letz R, Spengler JD. Estimating human exposures to nitrogen dioxide. An indoor-outdoor modeling approach. Environ Res 1983; 32:151-66.

173. Jakab GJ. Nitrogen dioxide-induced susceptibility to acute respiratory illness: a perspective. Bull NY Acad Med 1980; 56:847-56.

174. Dawson SV, Schencker MB. Health effects of inhalation of ambient concentrations of nitrogen dioxide. Am Rev Respir Dis 1979; 120:281-92.

175. Morrow PE. Toxicological data on NO_2: an overview. J Toxicol Environ Health 1984; 13:205-27.

176. Orehek J, Massari JP, Gayrard P, Grimaud C, Charpin J. Effect of short-term, low level nitrogen dioxide exposure on bronchial sensitivity of asthmatic patients. J Clin Invest 1976; 57:301-7.

177. Bauer MA, Utell MJ, Morrow PE, Speers DM, Gibb FR. 0.30 ppm nitrogen dioxide inhalation potentiates exercise-induced bronchospasm in asthmatics (abstract). Am Rev Respir Dis 1984; 129(Suppl:A151).

178. Melia RJ, Florey CV, Altman DG, Swan AV. Association between gas cooking and respiratory disease in children. Br Med J 1977; 2:149-52.

179. Melia RJ, Florey CV, Chinn S. The relation between respiratory illness in primary schoolchildren and the use of gas for cooking. I. Results from a national survey. Int J Epidemiol 1979; 8:333-8.

180. Florey CV, Melia RJ, Chinn S, *et al.* The relation between respiratory illness in primary schoolchildren and the use of gas for cooking. III. Nitrogen dioxide, respiratory illness and lung function. Int J Epidemiol 1979; 8:347-53.

181. Melia RJ, Florey CV, Morris RW, *et al.* Childhood respiratory illness and the home environment. II. Association between respiratory illness and nitrogen dioxide, temperature and relative humidity. Int J Epidemiol 1982; 11:164-9.

182. Melia RJ, Florey C, Sittampalam Y, Watkins C. The relation between respiratory illness in infants and gas cooking in the UK: a preliminary report. Proceedings of the 6th World Congress on Air Quality 16-20 August 1983, Paris: International Union of Air Pollution Prevention Associations, 1983; 263-9.

183. Ogston SA, Florey CV, Walker CH. The Tayside infant morbidity and mortality study: effect on health of using gas for cooking. Br Med J 1985; 290:957-60.

184. Keller MD, Lanese RR, Mitchell RI, Cote RW. Respiratory illness in households using gas and electricity for cooking. I. Survey of incidence. Environ Res 1979; 19:495-503.

185. Keller MD, Lanese RR, Mitchell RI, Cote RW. Respiratory illness in households using gas and electricity for cooking. II. Symptoms and objective findings. Environ Res 1979; 19:504-15.

186. Speizer FE, Ferris B Jr, Bishop YM, Spengler J. Respiratory disease rates and pulmonary function in children associated with NO_2 exposure. Am Rev Respir Dis 1980; 121:3-10.

187. Speizer FE, Ferris B Jr, Bishop YM, Spengler J. Health effects of indoor NO_2 exposure: preliminary results. In: Lee SD, ed. Nitrogen oxides and their effects on health. Ann Arbor, MI: Ann Arbor Science Publishers, Inc., 1980; 343-59.

188. Dodge R. The effects of indoor pollution on Arizona children. Arch Environ Health 1982; 37: 151-5.

189. Schenker MB, Samet JM, Speizer FE. Risk factors for childhood respiratory disease: the effect of host factors and home environmental exposures. Am Rev Respir Dis 1983; 28:1038-43.

190. Berwick M, Zagraniski RT, Leaderer BP, Stolwijk JA. Respiratory illness in children exposed to unvented combustion sources. In: Berglund B, Lindvall T, Sundell J, eds. Indoor air. Vol. 2, Radon, passive smoking, particulates and housing epidemiology. Stockholm: Swedish Council for Building Research, 1984; 255-60.

191. Hoek G, Brunekreef B, Meijer R, Scholten A. Indoor NO_2 and respiratory symptoms of Rotterdam children. In: Berglund B, Lindvall T, Sundell J, eds. Indoor air. Vol. 3, Sensory and hyperreactivity reactions to sick buildings. Stockholm: Swedish Coucil for Building Research, 1984; 227-32.

192. Hasselblad V, Humble CG, Graham MG, Anderson HS. Indoor environmental determinants of lung function in children. Am Rev Respir Dis 1981; 123:479-85.

193. Vedal S, Schenker MB, Samet JM, Speizer FE. Risk factors for childhood respiratory disease. Am Rev Respir Dis 1984; 130:187-92.

194. Fischer P, Remijn B, Brunekreef B, Van der Lende R, Shouten J, Quanjer P. Indoor air pollution and its effect on pulmonary function of adult non-smoking women: II. Associations between nitrogen dioxide and pulmonary function. Int J Epidemiol 1985; 14:221-6.

195. Comstock GW, Meyer MB, Helsing KJ, Tockman MS. Respiratory effects of household exposures to tobacco smoke and gas cooking. Am Rev Respir Dis 1981; 124:143-8.

196. Helsing KJ, Comstock GW, Meyer MB, Tockman ML. Respiratory effects of household exposure to tobacco smoke and gas cooking on nonsmokers. Environ Int 1982; 8:365-70.

197. Love GJ, Lan SP, Shy CM, Riggan WB. Acute respiratory illness in families exposed to nitrogen dioxide ambient air pollution in Chattanooga, Tennessee. Arch Environ Health 1982; 37:75-80.

198. Lebowitz MD, O'Rourke MK, Dodge R, *et al.* The adverse health effects of biological aerosols, other aerosols, and indoor microclimate on asthmatics and nonasthmatics. Environ Int 1982; 8:375-80.

199. Lebowitz MD, Holberg CJ, Boyer B, Hayes C. Respiratory symptoms and peak-flow associated with indoor and outdoor air pollutants in the Southwest. J Air Pollut Control Assoc 1985; 35:1154-8.

200. Kasuga H. A review of urinary hydroxyproline as a biochemical marker on health effects of smoking and air pollution with nitrogen dioxide. Tokai J Exp Clin Med 1985; 10:439-44.

201. Matsuki H, Kasuga H, Osaka F, Yanagisawa Y, Nishimura H. A comparative study on the health effects of smoking and indoor air pollution in summer and winter. Tokai J Exp Clin Med 1985; 10: 427-37.

202. Ozkaynak H, Ryan PB, Spengler JD, Letz R. Bias due to misclassfication of personal exposures in epidemiologic studies of indoor and outdoor air pollution. Presented at the Air Pollution Control Association and American Society for Quality Control Specialty Conference on quality assurance in air pollution measurements, 14-18 October 1984, Boulder, Colorado.

203. Vedal S. Epidemiological studies of childhood illness and pulmonary function associated with gas stove use. In: Gammage RB, Kaye SV, eds. Indoor air and human health. Chelsea, MI: Lewis Publishers, 1985; 303-16.

204. National Research Council, Committee on Medical and Biologic Effects of Environmental Pollutants, Subcommittee on carbon monoxide. Carbon monoxide. Washington, D.C.: National Academy of Sciences, 1977.

205. Coburn RF. Mechanisms of carbon monoxide toxicity. Prev Med 1979; 8:310-22.

206. Sterling TD, Dimich H, Kobayashi D. Use of gas ranges for cooking and heating in urban dwellings. J Air Pollut Control Assoc 1981; 32: 162-5.

207. Nagda NL, Koontz MD. Microenvironmental and total exposures to carbon monoxide for three population subgroups. J Air Pollut Control Assoc 1985; 35:134-7.

208. Caceres T, Soto H, Lissi E. Indoor house pollution: appliance emissions and indoor ambient concentrations. Atmos Environ 1983; 17:1009-13.

209. Cox BD, Wichelow MJ. Carbon monoxide levels in the breath of smokers and nonsmokers: effect of domestic heating systems. J Epidemiol Community Health 1985; 39:75-8.

210. Iglewicz R, Rosenman KD, Iglewicz B, O'Leary K, Hockemeier R. Elevated levels of carbon monoxide in the patient compartment of ambulances. Am J Public Health 1984; 74:511-12.

211. Cortese AD, Spengler JD. Ability of fixed monitoring stations to represent personal carbon monoxide exposures. J Air Pollut Control Assoc 1976; 26:1144-50.

212. Wallace LA. Use of personal monitor to measure commuter exposure to carbon monoxide in vehicle passenger compartment. Paper No. 79-59.2 Presented at Annual Meeting, Air Pollution Control Association, 24-29 June 1979, Cincinnati, Ohio.

213. Akland GG, Hartwell TD, Johnson TR, Whitmore RW. Measuring human exposure to carbon monoxide in Washington, D.C., and Denver, Colorado, during the winter of 1982-1983. Environ Sci Technol 1985; 19:911-8.

214. Wallace LA. Carbon monoxide in air and breath of employees in an underground office. J Air Pollut Control Assoc 1983; 33:678-82.

215. Kuller LH, Radford EP. Epidemiological bases for the current ambient carbon monoxide standards. Environ Health Perspect 1983; 52:131–9.

216. Aronow WS. Carbon monoxide and cardiovascular disease. Compr Ther 1983; 9:21–6.

217. Dolan MC. Carbon monoxide poisoning. Can Med Assoc J 1985; 133:392–7.

218. Ginsberg MD. Carbon monoxide intoxication: clinical features, neuropathology and mechanisms of injury. J Toxicol Clin Toxicol 1985; 23:281–8.

219. Barrett L, Danel V, Faure J. Carbon monoxide poisoning, a diagnosis frequently overlooked. J Toxicol Clin Toxicol 1985; 23:309–13.

220. Kelley JS, Sophocleus GJ. Retinal hemorrhages in subacute carbon monoxide poisoning. Exposures in homes with blocked furnaces. JAMA 1978; 239:1515–7.

221. Ferguson LS, Burke MJ, Choromokos EA. Carbon monoxide retinopathy. Arch Opthalmol 1985; 103:66–7.

222. Office of Technology Assessment. Wood use: U.S. competitiveness and technology, Vol. 11. Washington, D.C.: U.S. Government Printing Office, 1984. OTA-M-224.

223. Cooper JA. Environmental impact of residential wood combustion emissions and its implications. J Air Pollut Control Assoc 1980; 30:855–61.

224. Traynor GW, Apte MG, Carruthers AR, Dillworth JF, Grimsrud DT, Gundel LA. Indoor air pollution due to emission from woodburning stoves. Berkeley, CA: Lawrence Berkeley Laboratories, 1986 (LBL No. 17854).

225. Sexton K, Spengler JD, Treitman RD. Effects of residential wood combustion on indoor air quality: a case study in Waterbury, Vermont. Atmos Environ 1984; 18:1371–83.

226. Moschandreas DJ, Zabransky J Jr, Rector HE. The effects of woodburning on the indoor residential air quality. Environ Int 1980; 4:463–8.

227. Hytonen S, Alfheim I, Sorsa M. Effect of emissions from residential wood stoves on SCE induction in CHO cells. Mutat Res 1983; 118:69–75.

228. Alfheim I, Ramdahl T. Contribution of wood combustion to indoor air pollution as measured by mutogenicity in *salmonella* and polycyclic aromatic hydrocarbon concentration. Environmental Mutagenesis 1984; 6:121–30.

229. Fick RB, Paul ES, Merrill WW, Reynolds HY, Loke JSO. Alterations in the antibacterial properties of rabbit pulmonary macrophages exposed to wood smoke. Am Rev Respir Dis 1984; 129:76–81.

230. Wong KL, Stock MF, Malek DE, Alarie Y. Evaluation of the pulmonary effects of wood smoke in guinea pigs by repeated CO_2 challenges. Toxicol Appl Pharmacol 1984; 75:69–80.

231. Pandey MR. Prevalence of chronic bronchitis in a rural community of the hill region of Nepal. Thorax 1984; 39:331–6.

232. Pandey MR. Domestic smoke pollution and chronic bronchitis in a rural community of the hill region of Nepal. Thorax 1984; 39:337–9.

233. Pandey MR, Regmi HN, Neupane RP, Gautam A, Bhandari DP. Domestic smoke pollution and respiratory function in rural Nepal. Tokai J Exp Clin Med 1985; 10:471–81.

234. Master KM. Air pollution in New Guinea. Cause of chronic pulmonary disease among stone-age natives in the highlands. JAMA 1974; 228: 1653–5.

235. Anderson HR. Respiratory abnormalities, smoking habits and ventilatory capacity in a highland community in Papua New Guinea: prevalence and effect on mortality. Int J Epidemiol 1979; 8:127–35.

236. Anderson HR. Respiratory abnormalities in Papua New Guinea children: the effects of locality and domestic wood smoke pollution. Int J Epidemiol 1978; 7:63–72.

237. Kossove D. Smoke-filled rooms and lower respiratory disease in infants. S Afr Med J 1982; 61:622–4.

238. Dekoning HW, Smith KR, Last JM. Biomass fuel combustion and health. Bull WHO 1985; 63:11–26.

239. Smith KR, Aggarwal AL, Dave RM. Air pollution and rural biomass fuels in developing countries: a pilot village study in India and implications for research and policy. Atmos Environ 1983; 17: 2343–62.

240. Honicky RE, Akpom CA, Osborne JS. Infant respiratory illness and indoor air pollution from a woodburning stove. Pediatrics 1983; 71:126–8.

241. Honicky RE, Osborne JS III, Akpom CA. Symptoms of respiratory illness in young children and the use of wood-burning stoves for indoor heating. Pediatrics 1985; 75:587–93.

242. Tuthill RW. Woodstoves, formaldehyde, and respiratory disease. Am J Epidemiol 1984; 120: 952–5.

243. Peters HA, Croft WA, Wooson EA, Darcey BA, Olson MA. Seasonal arsenic exposure from burning chromium-copper-arsenate-treated wood. JAMA 1984; 251:2392–6.